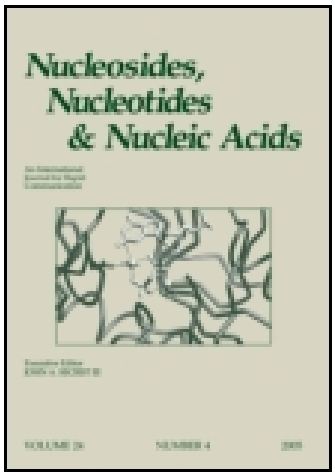

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SYNTHESIS OF THIAAZAHETEROCYCLE NUCLEOSIDE ANALOGUES

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ABSTRACT

The syntheses of thiazinone, thiazinedione and thiazolinone base modified nucleoside analogues have been discussed in both the deoxy- and ribosyl series. Both inter- and intramolecular *N*-glycosylations were evaluated.

In recent years, the search to discover potent and selective antiviral or anticancer agents has resulted in the design of nucleoside analogues with modifications on the heterocyclic aglycone moiety. Some examples have shown that the structure of the nucleobase can be changed considerably while retaining the biological interest.[1] In particular, *N*-[2] and *C*-[3]linked nucleosides tethered to five and six membered modified azaheterocycles exhibiting biological activity have aroused new attention. We proposed the synthesis of nucleosides incorporating novel thiaazaheterocycles having structural analogies with the natural nucleobases. Modified 3′-thiaazaheterocycle

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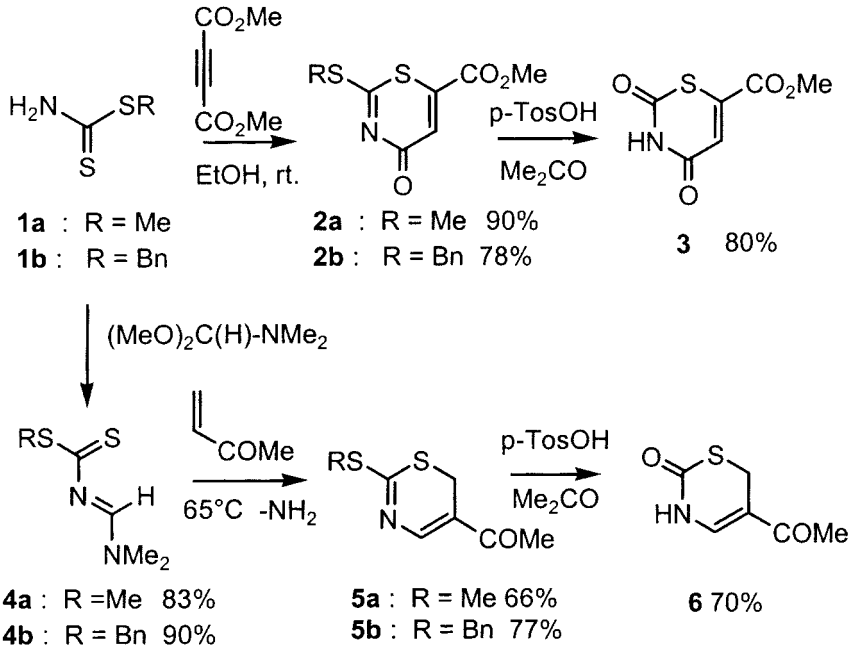
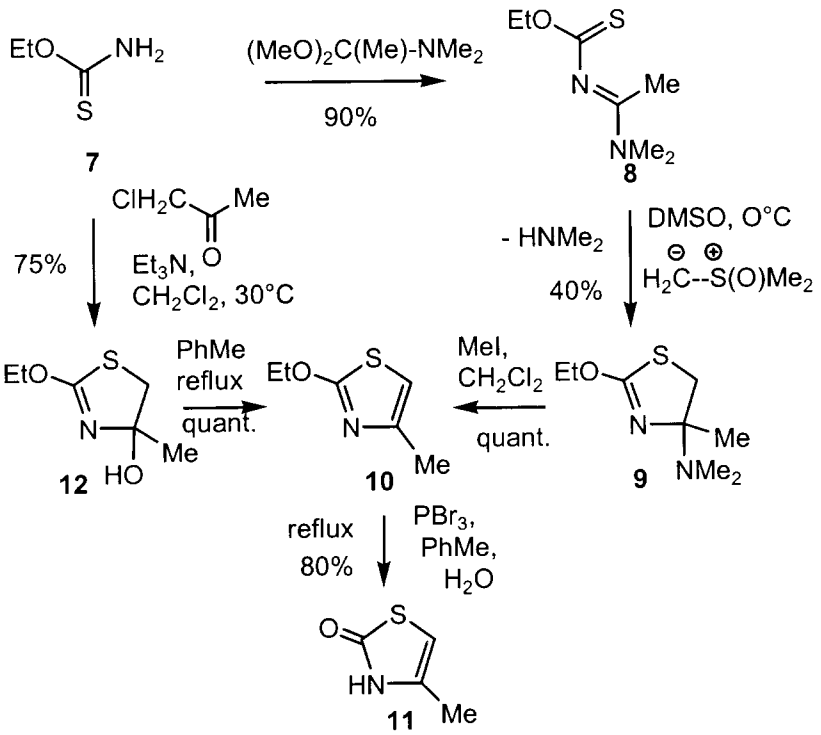
nucleoside analogues have been already synthetized from 3′-thiaazabutadiene thymidine precursors.[4] Here, the elaboration of *N*-deoxy- and *N*-ribonucleosides has been investigated by *N*-glycosylation with thiazinone, thiazinedione and thiazolinone heterocycles. An intramolecular glycosylation process was also attempted to achieve stereoselectivity with the *N*-deoxyribosyl analogues.

The preparation of thiaazaheterocycle analogues can be achieved from 4-dimethylamino-1-thia-3-aza-but-1,3-dienes (*N*-thioacylamidine) or from their thiocarbamate intermediates.[5] 6-Methoxycarbonyl-1,3-thiazin-2,4-dione **3** was prepared from the dithiocarbamate **1** (Sch. 1). [3 + 3] Cycloaddition of **1a** and **1b** with dimethyl acetylenedicarboxylate gave the corresponding thiazinones **2a** and **2b** in 90% and 78% yield, respectively. Hydrolysis of the imines **2a**–**b** using *p*-toluensulfonic acid in acetone afforded the thiazin-2,4-dione **3** (80%).

The 5-acetyl-3,6-dihydro-1,3-thiazin-2-one **6** was synthesized from the thiaazabutadienes **4a** and **4b**. Condensation of thiocarbamates **1a** and **1b** with *N,N*-dimethylformamide dimethylacetal leads to the formation of thiaazabutadienes **4a** (83%) and **4b** (90%) respectively, which afforded the thiazines **5a** (66%) and **5b** (77%) upon [4 + 2] cycloaddition with methyl vinyl ketone. Hydrolysis of these thiazines with *p*-TSAgave the targeted thiazin-2-one **6** in 70% yield.



Scheme 1.

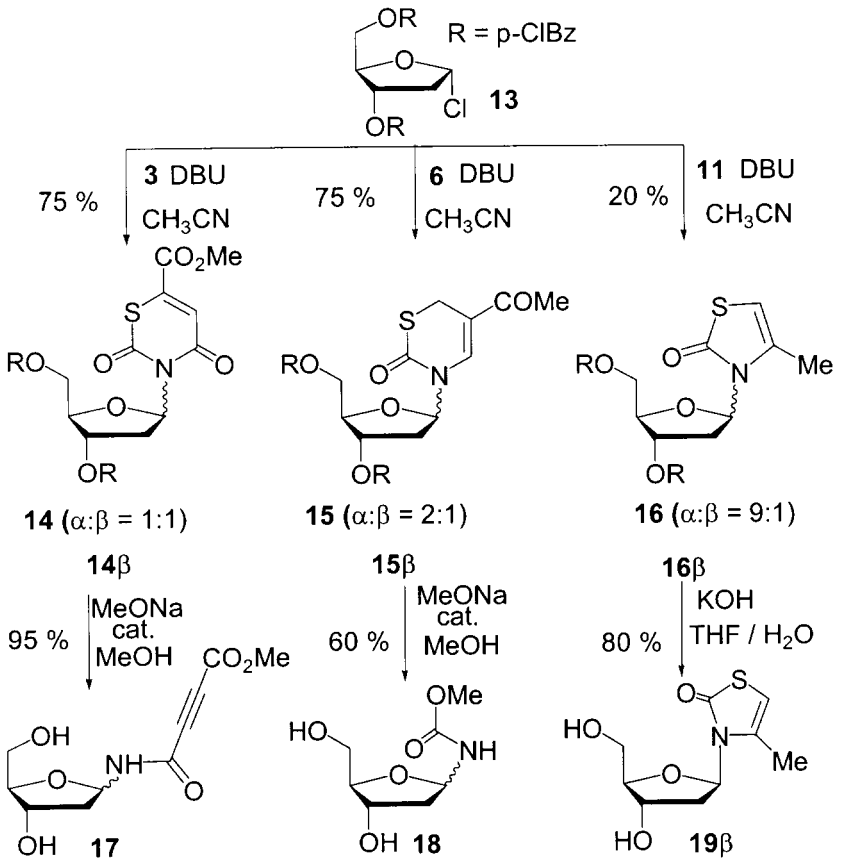


Scheme 2.

The synthesis of 4-methyl 2*H*-1,3-thiazolin-2-one **11** was achieved from 2-ethoxy-4-methyl-*N*-thioacylamidine **8** (Sch. 2). Condensation of ethyl-thiocarbamate **7** with *N,N*-dimethylacetamide dimethylacetal afforded the *N*-thioacylamidine **8**, in quantitative yield, and furnished the thiazol-2-ine **9** upon [4 + 1] heterocyclisation with the trimethyl sulphonium ylide,[5e] in 40% yield. Addition of methyl iodide resulted in quantitative aromatisation of compound **9** to form thiazole **10** which was converted to the target thiazolinone **11**[6] (80%) by treatment with phosphorus tribromide (**10** remains stable under usual acidic hydrolysis).

The yield of thiazole **10** was improved by an alternate route *via* the thiazoline **12**. The reaction of the thiocarbamate **7** with chloroacetone gave the thiazoline **12**, in 75% yield, which was quantitatively transformed into the thiazole **10** in refluxing toluene.

The nucleoside derivatives were synthesized from two haloribosyl precursors: 3,5-di-*O*-benzoyl-2-deoxy-ribofuranosyl chloride[7] **13** and 5-*O*-*tert*-butyldiphenylsilyl-2,3-*O*-isopropylidene-ribofuranosyl chloride[8] **28**, chosen as glycosyl donors. *N*-Glycosylations with deoxyribosyl chloride **13** and thiaazanucleobase analogues **3**, **6** and **11** were firstly attempted in the presence of DBU (1.1 eq.) leading to the corresponding deoxynucleosides **14**

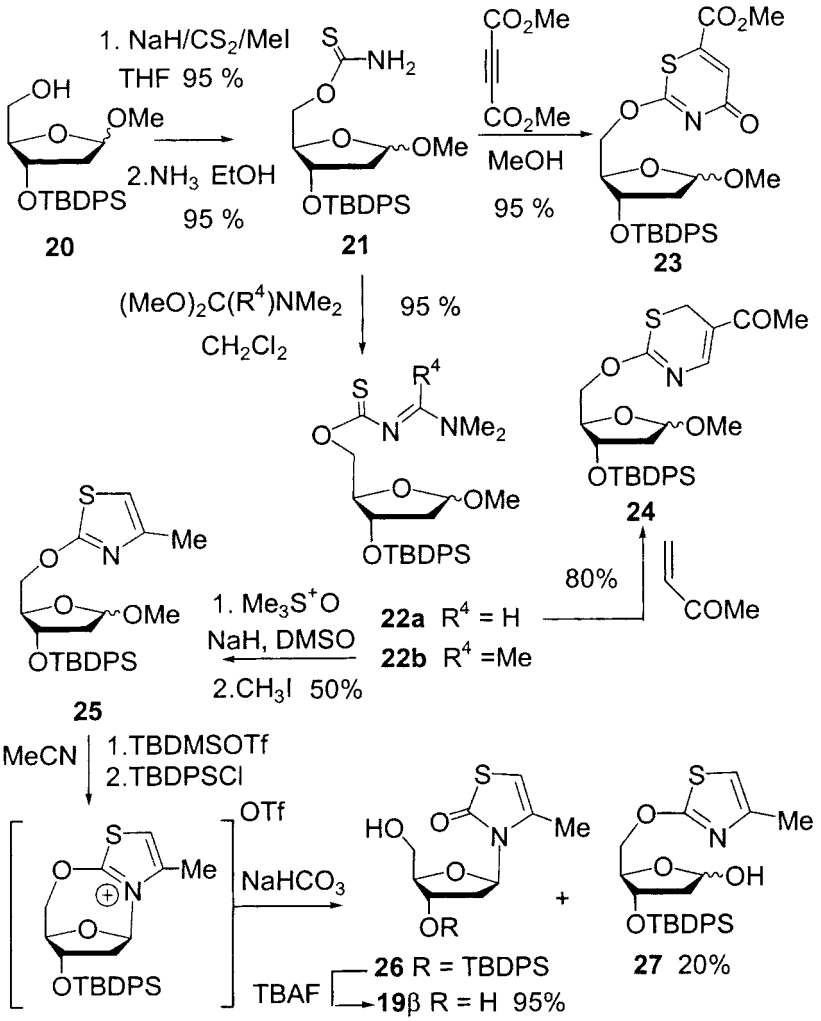


Scheme 3.

(75%), **15** (75%) and **16** (20%), respectively (Sch. 3). Anomeric deoxynucleosides **14** and **15** were isolated in 1:1 and 2:1, α:β ratio, respectively, whereas, thiazolinone analogue **16** was obtained in 9:1, α:β ratio.

Attempts to remove the *p*-chlorobenzoyl group in thiazinone deoxynucleosides **14** and **15** under basic conditions induced partial degradation leading to ring opening of the heterocycle moiety. Treatment of **14**β and **15**β with catalytic amount of MeONa afforded the formation of anomeric mixture of *N*-amidoacetylenic ribosyl **17** (95%) and *N*-carbamate ribosyl **18** (60%), respectively. However, no such degradation was observed with thiazolone **16**β which on treating with KOH gave the desired deoxynucleoside **19**β (80%).

The results obtained in the deoxynucleoside series prompted us to investigate an alternative strategy involving a stereoselective intramolecular transposition.[9] Following this hypothesis, the primary target appeared to be the elaboration of the thiaazaheterocycles at the 5′-position of a deoxyriboside precursor (Sch. 4).



Scheme 4.

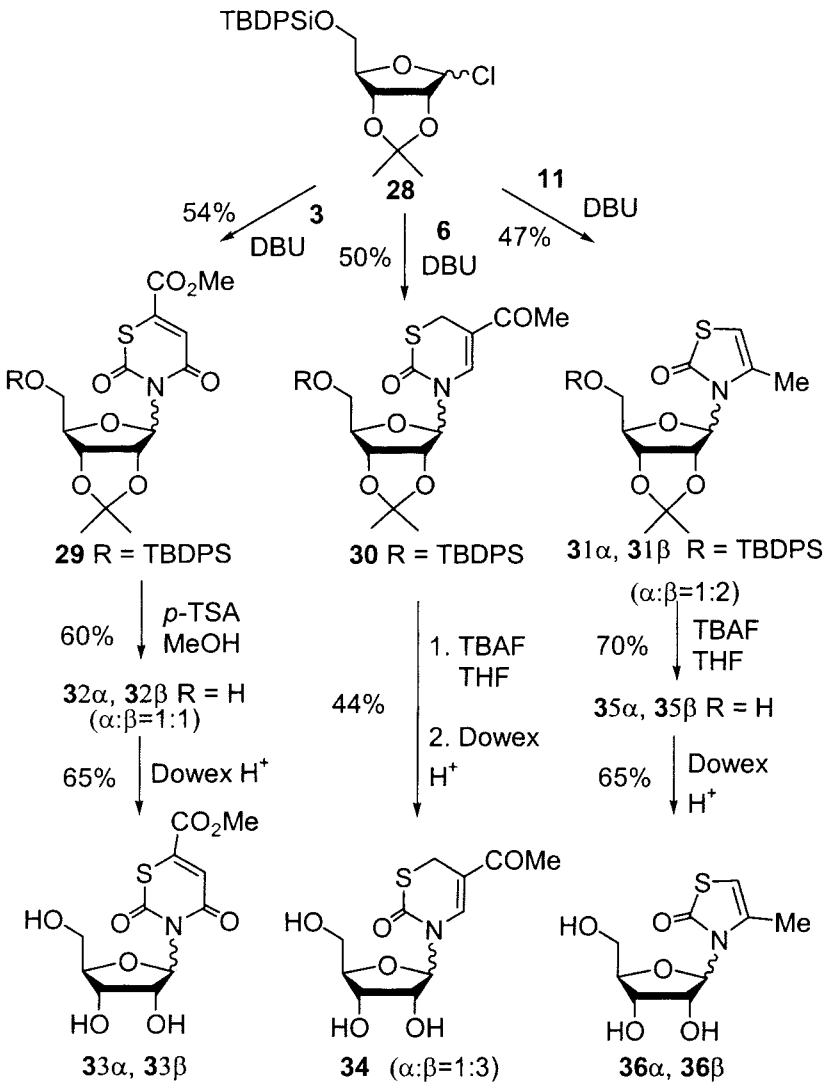
Methyl 3′-*tert*-butyldiphenylsilyl-5′-thiocarbamate-deoxyriboside **21** was prepared from methyl 3′-*tert*-butyldiphenylsilyl-deoxyriboside **20** in 95% yield. Following a similar protocol as mentioned in the synthesis of *N*-thioacylamidines (Sch. 2), reaction of thiocarbamate deoxyriboside **21** with *N,N*-dimethylformamide dimethylacetal and *N,N*-dimethylacetamide dimethylacetal, led to the 5′-thiaazabutadienes **22a** and **22b**, in 95% yields. The 5′-thiaazaheterocycle isodeoxynucleosides **23** (70%), **24** (80%) and **25** (50%), were formed by cycloaddition reactions as previously discussed from the thiocarbamate **21** and from the dienes **22a** and **22b**, respectively.

Attempts to achieve the 5′,1′-transposition of 5′-thiazinone deoxyribosides **23** and **24** using various Lewis acids[9] resulted in the hydrolysis of the imine function without occurrence of *N*-glycosylation. However, partial success was achieved with 5′-thiazole deoxyriboside **25** using silyl triflates initiating an intramolecular rearrangement. Thiazole deoxyriboside **25** was treated twice with *tert*-butyldimethylsilyl trifluoromethanesulfonate (2.2 eq) along with supplementary amount of *tert*-butyldiphenylsilyl chloride (2 eq). Subsequent hydrolysis of the anhydroammonium intermediate with sodium carbonate competitively gave the desired β-deoxynucleoside **26** (20%) along with ribofuranose **27** (20%) and unreacted starting material **25** (41%). The use of a higher amount of catalysts improved the yield of the furanose **27**. Unfortunately no improvement in the transposition process was observed using other catalysts. Due to the nature of the thiaazaheterocycle change of the anomeric group by a more labile thioether activating group is either not suitable. However, the deoxynucleoside **26** was isolated as a single diastereoisomer and its β-configuration was confirmed by nOe experiment.[10] Finally, the deprotection of compound **26** in the presence of tetrabutylammonium fluoride led to the desired deoxynucleoside **19**β in 95% yield.

The synthesis of nucleoside analogues was then extended to the ribonucleosides. *N*-Glycosylations of the ribofuranosyl chloride **28** with heterocycles **3**, **6** and **11** in the presence of DBU (1.1 eq.) led to a mixture of corresponding anomeric nucleosides **29** (54%, α:β ratio: 1/1), **30** (50%, α:β ratio: 1/3) and **31** (47%, α:β ratio: 1/2), respectively (Sch. 5).

Deprotection of nucleoside analogues **29** (mixture) and purified thiazole anomers **31**α and **31**β was carried out in two steps: i) treatment of **29** with p-TSA to get the α- and β-ribosyls **32**α and **32**β (60%), which were isolated in 1:1 α:β ratio, and treatment of **31** with tetrabutylammonium fluoride to get the corresponding 5′-OH intermediates **35**α and **35**β (70%) (TBAF induce degradation in case of **29**). ii) Hydrolysis of the ketal group in **32**α, **32**β, **35**α and **35**β with Dowex H^+ resin to get the free nucleosides **33**α, **33**β, **36**α and **36**β in 65% yield. Treatment of anomeric mixture of **30** was carried out without purification following a similar procedure to afford an α,β-anomeric mixture of the corresponding free nucleoside **34** in 44% overall yield (α:β ratio 1:3).

In conclusion, we have designed the synthesis of thiaazaheterocycle base modified nucleoside analogues in both deoxy- and ribofuranosyl series. *N*-Glycosylation between halogenofuranosyls and thiaazaheterocycles seems to be the most efficient process to produce corresponding nucleoside derivatives. Nevertheless, intermolecular stereoselective glycosylation remains attractive for the stereoselective synthesis of deoxyribonucleosides. No significant antiviral activity of these nucleoside analogues measured on CEM4 lymphocytic cell lines infected with HIV-1 (Lai strain) has been observed.



Scheme 5.

Experimental Data

^{1}H and ^{13}C spectra were obtained on Bruker ARX 400 or Bruker AC200. Chemical shifts (δ) are given in ppm relative to the TMS (tetramethylsilane). The ^{1}H-^{1}H coupling constants (J) were measured in Hz. Mass spectra were recorded on a HP 5889 A quad spectrometer or a ZabSpecE-TOF spectrometer for high resolution spectra. Infrared spectra were recorded on a Bruker IFS 45 WHR spectrometer Melting points were determined with a RCH (C. Reichert) melting point apparatus. Specific rotations were

measured at 20°C using a Polar 341 Perkin-Elmer. Thin layer chromatography were performed on Merck 60 F_{254} coated plates. Silica gel chromatography were performed with 0.04–0.06 mm silica gel. All the solvents were purified using standard procedures.[11]

6-Methoxycarbonyl-2-methylthio-4*H*-1,3-thiazin-4-one (2a) and 2-Benzylthio-6-methoxycarbonyl-4*H*-1,3-thiazin-4-one (2b). General procedure. To a solution of thiocarbamate **1a–b** (10.91 mmol) in ethanol, dimethyl acetylenedicarboxylate (1.6 mL, 13.09 mmol) was added with stirring, stirring was continued 1 h at room temperature. The product was isolated by filtration and washed with ethanol. The crude solid was recrystallized from ethanol to get **2a–b**. **(2a)** 90% yield: m.p. 140–141°C. ^{1}H NMR($CDCl_3$; 200 MHz) δ: 2.85 (s, 3H); 3.87 (s, 3H); 6.96 (s, 1H, H5). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 16.3 (CH_3S); 52.9 (CH_3O); 120 (C-5); 144.2 (C-6); 166 (C=O ester); 177.9 (C-2); 199.98 (C-4). MS (EI) M/z (%): $M^+ = 217$; 203 (82); 144 (70); 116 (100); 86 (70); 57 (55). I.R. KBr (ν cm^{-1}) 1702; 1458; 1337; 1213; 1002. (**2b**) 78% yield: m.p. 106–107°C. ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 3.86 (s, 3H); 4.68 (s, 2H); 6.98 (s, 1H, H5); 7.37 (m, 5H, HAr). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 38.2 (CH_2S); 52.9 (CH_3O); 120.2 (C-5); 128.3 to 134.3 (C-Ar); 144.0 (C-6); 166.0 (C=O ester); 177.9 (C-2); 196.7 (C-4). MS (EI) M/z (%): $M^+ = 293$; 116 (29); 91 (100); 65 (38). I.R. KBr (ν cm^{-1}) 1717; 1686; 1462; 1332; 1209; 1160; 1004; 719.

6-Methoxycarbonyl-4*H*-1,3-thiazin-2,4-dione (3). To a solution of **2a–c** (3.41 mmol) in acetone (30 mL) was added *p*-toluene sulfonic acid monohydrate (0.65 g, 3.41 mmol). The mixture was stirred for 6 h at room temperature, 100 mL of water and 100 mL of ethyl acetate were added. After extraction, the organic layer was washed with brine, dried over magnesium sulfate, filtered and then evaporated to dryness. The product was purified by flash chromatography on silica gel eluting with petroleum ether/ethyl acetate (8/2) and recrystallized from dichloromethane to get **3** in 80% yield. m.p. 168–169°C. ^{1}H NMR (acetone-d_6; 200 MHz) δ: 3.85 (s, 3H); 6.87 (s, 1H); 11.34 (NH). ^{13}C NMR (acetone-d_6; 50 MHz) δ: 53 (CH_3O); 118.3 (C-5); 143.7 (C-6); 166.1 (C=O ester); 166.4 (C-4); 169.3 (C-2). MS (EI) M/z (%): $M^+ = 187$ (32); 144 (63); 116 (84); 86 (45); 85 (100); 59 (45); 57 (83); 49 (25). I.R. KBr (ν cm^{-1}) 3209; 1761; 1721; 1677; 1339; 1220. Anal. Calcd for $C_6H_5NO_4S$: C, 38.50; H, 2.69; N, 7.48; S, 17.13. Found: C, 38.43; H, 2.80; N, 7.33; S, 17.09.

4-*N,N*-dimethylamino-2-methylthio-1-thia-3-aza-1,3-butadiene (4a). *N,N*-dimethylformamide dimethyl acetal (2.12 mL, 16 mmol) was added to the thiocarbamate **1a** (1.71 g, 16 mmol). The mixture was stirred for 1 h at room temperature. After removal of the methanol formed, the crude product was purified by flash chromatography on silica gel eluting with petroleum

ether/ethyl acetate (8/2) to get **4a** in 83% yield. m.p. 83–84°C. ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 2.6 (s, 3H, CH_3S); 3.17, 3.24 2*(s, 3H, $N(CH_3)_2$); 8.68 (s,1H, H4). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 36.1 ($N(CH_3)_2$); 41.7 (CH_3S); 156.9 (C-4); 220.99 (C=S). MS (EI) M/z (%): $M^+ = 162$; 115 (100); 99 (23); 71 (44); 44 (40); 42 (50). I.R. KBr (ν cm^{-1}) 1619; 1412; 1313; 1260; 1204; 1121; 983; 951.

2-Benzylthio-4-*N,N*-dimethylamino-1-thia-3-aza-1,3-butadiene (4b). Same experimental conditions as described for **4a**, starting from thiocarbamate **1b** gave **4b** in 90% yield. m.p. 93–94°C. ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 3.09, 3.12 2*(s, 3H, $N(CH_3)_2$); 4.47 (s, 2H, CH_2S); 7.237.32 (m, 5H, HAr); 8.62 (s,1H, H4). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 36.1 (CH_2S); 40.0, 40.6 ($N(CH_3)_2$); 126.8 to 137 (C-Ar); 157.2 (C-4); 218.6 (C=S). MS (EI) M/z (%): $M^+ = 238$; 115 (100); 99 (21); 91 (33). I.R. KBr (ν cm^{-1}) 1635; 1624; 1472; 1344; 1338; 960; 723.

5-Acetyl-2-methylthio-6*H*-1,3-thiazine (5a). *N*-thioacylamidine **4a** (3 g, 18.49 mmol) was heated with methyl vinyl ketone (15 mL, 184.7 mmol) at 65°C for 72 h. After removal of the solvent in vacuo, the crude product was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate (8/2), to get **5a** in 66% yield. m.p. 66°C. ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 2.39 (s, 3H, CH_3S); 2.57 (s, 3H, CH_3); 3.60 (s, 2H,H-6); 7.71 (s, 1H, H4). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 14.5 (CH_3); 22.2 (CH_2S); 25 (CH_3S); 115.8 (C-5); 145 (C-4); 170.1 (C-2); 195.5 (C=O). MS (EI) M/z (%): $M^+ = 187$; 145 (90), 144 (29), 71 (17), 43 (100); 39 (15), 28 (30).

5-Acetyl-2-benzylthio-6*H*-1,3-thiazine (5b). Same experimental conditions as described for **5a**, starting from thiocarbamate **4b** gave **5b** in 77% yield. m.p. 86–87°C. ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 2.39 (s, 3H); 3.6 (s, C-6); 4.43 (s, 2H, CH_2S); 7.37–7.33 (m, 5H, HAr); 7.86 (s, 1H, H4). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 22.6 (CH_3); 25.4 (C-6); 36.1 (CH_2S); 116.1 (C-5); 127.6 to 136.2 (C-Ar); 145.97 (C-4); 160.6 (C-2); 195.9 (C=O). MS (EI) M/z (%): $M^+ = 263$; 123 (15), 91 (66), 71 (62), 65 (18), 43 (100), 42 (40), 41 (42), 39 (23), 31 (22), 29 (39), 27 (27).

5-Acetyl-3,6-dihydro-2*H*-1,3-thiazin-2-one (6). Same experimental conditions as described for **3**, starting from **5a**–**b** gave **6** in 70% yield. m.p. 159–160°C. ^{1}H NMR (acetone-d_6; 200 MHz) δ: 2.3 (s, 3H); 3.88 (s, 2H); 7.52 (s, 1H, H4); 9.32 (NH). ^{13}C NMR (acetone-d_6; 50 MHz) δ: 24.8 (CH_3); 112.6 (C-5); 139.5 (C-4); 167.6 (C-2); 194.4 (C=O). MS (EI) M/z (%): $M^+ = 157$; 115 (16); 86 (14); 82 (24); 70 (18); 55 (69); 54 (53); 43 (100); 39 (16); 28 (51). I.R. KBr (ν cm^{-1}) 3226; 3084; 1685; 1626; 1305; 1204. Anal. Calcd for $C_6H_5NO_2S$: C, 45.85; H, 4.49; N, 8.91; S, 20.40. Found: C, 45.74; H, 4.44; N, 9.05; S, 20.69.

2-Ethoxy-4-methyl-4-(*N,N*-dimethylamino)-1-thia-3-aza-1,3-butadiene (8). *N,N*-dimethylacetamide dimethyl acetal (2.33 mL, 16 mmol) and thiocarbamate **7** (1.68 g, 16 mmol) were stirred for 1h at room temperature. After removal of the methanol under vacuo, the crude product was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate (8/2), to get **8** in quantitative yield. ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 1.36 (t, 3H, $C\underline{H}_3$-CH_2, J = 7.10); 2.43 (s, 3H, CH3); 3.12, 3.15 2*(s, 3H, $N(CH_3)_2$); 4.40 (q, 2H, $C\underline{H}_2$-CH_3, J = 7.10). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 14.0 (CH_3-CH_2); 17.4 (C4-CH_3); 38.4, 38.7 ($N(CH_3)_2$); 66.5 (CH_2); 164.9 (C-4); 196.6 (C=S).

2-Ethoxy-4-methyl-4-(*N,N*-dimethylamino)-thiazol-2-ine (9). A solution of trimethylsulphonium iodide (3.04 g, 14 mmol) in dry DMSO (30 mL) was added to sodium hydride (60% mineral oil dispersion) under argon (0.56 g, 14 mmol). The mixture was allowed to stir for 30 min. at room temperature, then **8** (2.44 g, 14 mmol) in solution in dry DMSO (8 mL) was added. The mixture was stirred for 1 h at room temperature and added to water (100 mL). The aqueous layer was extracted with diethyl ether (2*100 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated. The crude product was purified by flash chromatography on silica gel eluting with petroleum ether/ethyl acetate (7/3) to get **9** as an oil in 40% yield. ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 1.25 (t, 3H, $C\underline{H}_3$-CH_2, J = 7.20); 1.38 (s, 3H, CH3); 2.25 (s, 6H, $N(CH_3)_2$); 3.04 (d, 1H, H5a, $J_{5a-5b} = 11.29$); 3.44 (d, 1H, H5b, $J_{5b-5a} = 11.29$); 4.24 (q, 2H, $C\underline{H}_2$-CH_3, J = 7.20). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 14.4 ($\underline{C}H_3$-CH_2); 26.1 (CH_3); 39.0 ($N(CH_3)_2$); 41.3 (C-5); 66.9 (CH_2O); 93.7 (C-4); 163.8 (C-2).

2-Ethoxy-4-methyl-thiazole (10). A mixture of thiazoline **12** (0.29 g, 1.3 mmol) in toluene (5 mL) was heated for 2h at reflux. After removal of the solvent in vacuo, the crude product was purified by flash column chromatography on silica gel, eluting with petroleum ether/ethyl acetate (8/2), to get **10.** ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 1.40 (t, 3H, $C\underline{H}_3CH_2$, J = 7); 2.25 (d, 3H, CH_3, $J_{CH3-CH} = 1.22$); 4.41 (q, 2H, CH_2, J = 7); 6.18 (q, 1H, H5, $J_{CH3-CH} = 1.22$). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 14.2 ($\underline{C}H_3$); 17.6 ($\underline{C}H_3$-C_4); 62.7 ($\underline{C}H_2$); 104.4 (C-5); 146.5 (C-4); 173.8 (C-2). MS (EI) M/z (%): $M^+ = 143$; 115 (100); 87 (35); 71 (35); 70 (46); 46 (60); 45 (49); 42 (83); 29 (30); 27 (25). I.R. KBr (ν cm^{-1}) 2983; 1517; 1476; 1378; 1307; 1232; 1137; 1024.

4-Methyl-2*H-1,3-thiazolin-2-one (11).* To a solution of thiazole **10** (1 g, 3.41 mmol) in toluene (10 mL) was added phosphorus tribromide (0.2 mL, 2.38 mmol). The mixture was heated at reflux for 2 h and 2 mL of water was added. The mixture was cooled to room temperature and the aqueous layer was extracted with dichloromethane (100 mL). The organic layer was dried over magnesium sulfate, filtered and then concentrated. The crude product

was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate (5/5), yielded **11** in 80% yield. m.p. 73–74°C. ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 2.11 (d, 3H, CH_3, $J_{CH3–CH} = 1.22$); 5.68 (q, 1H, H5, $J_{CH3–CH} = 1.22$); 10.33 (NH). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 14.4 (CH_3); 97.5 (C-5); 130.8 (C-4); 176.4 (C-2). MS (EI) M/z (%): $M^+ = 115$; 91 (15); 87 (15); 71 (19); 46 (23); 45 (34); 42 (85). I.R. KBr (ν cm^{-1}) 3090; 1646; 1445; 1219. Anal. Calcd for C_4H_5NOS: C, 41.72; H, 4.38; N, 12.16; S, 27.84. Found: C, 41.43; H, 4.47; N, 11.61; S, 27.80.

2-Ethoxy-4-hydroxy-4-methyl-thiazol-2-ine (12). To a solution of thiocarbamate **7** (1 g, 0.094 mol) in dry dichloromethane (10 mL) were added triethylamine (2.7 mL, 0.19 mol) and chloroacetone (1.5 mL, 0.19 mol). The mixture was heated at 30°C for 24 h and diluted with water (100 mL). The aqueous layer was extracted with dichloromethane (2*100 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated. The crude product was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate (5/5), to get **12** in 75% yield. m.p. 86-88°C. ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 1.34 (t, 3H, J = 7.20, $\underline{C}H_3CH_2$); 1.61 (s, 3H, C4-CH_3); 3.35 (d, 1H, H5a, $J_{5a–5b} = 11.20$); 3.48 (d, 1H, H5b, $J_{5a–5b} = 11.20$); 4.29 (q, 2H, J = 7.20); 5.48 (1H, OH). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 14.3 ($\underline{C}H_3CH_2$); 29 (CH_3); 45.7 (C-5); 67.5 ($\underline{C}H_2O$); 101.0 (C-4); 168.3 (C-2). MS (EI) M/z (%): $M^+ = 161$; 146 (43); 118 (23); 86 (84); 43 (100); 29 (37). I.R. KBr (ν cm^{-1}) 3179; 2979; 1621; 1259; 1235; 1132.

3-(3,5-Di-*O*-*p*-chlorobenzoyl-2-deoxy-α,β-D-ribofuranosyl)-6-methoxycarbonyl-4*H*-1,3-thiazin-2,4-dione (14). To a solution thiazindione **3** (0.3 g, 1.6 mmol) in dry acetonitrile (10 mL) was added DBU (0.26 mL, 1.76 mmol). The mixture was cooled at 0°C and stirred for 15 min. before the addition of ribosyl chloride 13[7] (0.75 g, 1.76 mmol). The mixture was allowed to stir for 3 h at 0°C, and water (100 mL) was added. The solution was extracted with dichloromethane (2*100 mL) and the organic layers were washed with brine and dried over magnesium sulfate, filtered and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate (9/1), to get **14** in 60% yield (α/β ratio 1/1). The anomer **14**α was recrystallized from diethyl ether. α **anomer**: $[\alpha]_D^{20} = +21.9$; (C = 1.00, $CHCl_3$). ^{1}H NMR ($CDCl_3$; 400 MHz) δ: 2.79–2.84 (m, 1H, H2′a); 2.97–3.03 (m, 1H, H2′b); 3.87 (s, 3H, OCH_3); 4.46 (dd, 1H, H5′a, $J_{5'a–4'} = 3.60$ and $J_{5'a–5'b} = 11.90$); 4.63 (dd, 1H, H5′b, $J_{5'b–4'} = 4.80$ and $J_{5'a–5'b} = 11.90$); 4.89–4.92 (m, 1H, H4′); 5.44–5.55 (m, 1H, H3′); 6.23 (dd, 1H, H1′, J = 6.30 and 7.80); 7.03 (s, 1H, H5); 7.41, 7.43 (2d, 4H, J = 8.80, HAr); 7.92, 8.01 (2d, 4H, J = 8.80, HAr). ^{13}C NMR ($CDCl_3$; 100 MHz) δ: 34.5 (C-2′); 52.9 (OCH_3); 64.1 (C-5′); 73.9 (C-3′); 82.3 (C-4′); 82.7 (C-1′); 119.4 (C-5); 127.6 to 140.0 (C-Ar); 140.0 (C-4); 164.1, 168.5 (C-2, C-4); 164.9, 165.6 (C=O ester); 165.2 (C=O ester). β **anomer**: $[\alpha]_D^{20} = -21.8$ (C = 1.00, $CHCl_3$). m.p.

157–159°C. ^{1}H NMR ($CDCl_3$; 400 MHz) δ: 2.43–2.50 (m, 1H, H2′a); 3.21–3.29 (m, 1H, H2′b); 3.87 (s, 3H, OCH_3); 4.45–4.49 (m, 1H, H4′); 4.57 (dd, 1H, H5′a, J = 6 and 11.77); 4.66 (dd, 1H, H5′b, J = 5 and 11.77); 5.76–5.8 (m, 1H, H3′); 6.30 (dd, 1H, H1′, J = 6.34 and 7.39); 7.01 (s, 1H, H5); 7.38, 7.42 (2d, 4H, HAr, J = 8.55); 7.94, 7.99 (2d, 4H, HAr, J = 8.55). ^{13}C NMR ($CDCl_3$; 100 MHz) δ: 39.9 (C-2′); 52.9 (OCH_3); 64.1 (C-5′); 74.9 (C-3′); 82.3 (C-4′); 82.4 (C-1′); 119.6 (C-5); 127.7 to 140.1 (C-Ar); 140.1 (C-4); 163.9, 168.3 (C-2, C-4); 164.9, 165.4 (C=O ester); 165.6 (C=O ester). MS {(CI^+, NH_4^+), $M^+18 = 597$}; (EI) M/z (%): 267 (20); 141 (20); 139 (60); 81 (100). I.R. KBr (ν cm^{-1}) 1721; 1696; 1327; 1277; 1093; 1015; 761. Anal. Calcd for $C_{25}H_{19}Cl_2NO_9S$: C, 51.74; H, 3.30; Cl, 12.22; N, 2.41; S, 5.52. Found: C, 51.84; H, 3.42; Cl, 12.35; N, 2.32; S, 5.21. (LSIMS with Cs^+, Positif in Micromasse)–(Calcd.: $[M + H]^+$: 580.02367. Found: $[M + H]^+$: 580.0226

5-Acetyl-3-(3,5-di-*O*-*p*-chlorobenzoyl-2-deoxy-α,β-D-ribofuranosyl)-3,6-dihydro-2*H*-1,3-thiazin-2-one (15). The protected nucleoside **15** was obtained by following a similar procedure as in the preparation of **14**, from thiazinone **6** (0.5 g, 3.18 mmol) and ribosyl chloride **13**[7] (1.5 g, 3.5 mmol). The crude product was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate (8/2), to get **15** in 75% yield (α/β ratio 2/1). α **anomer** : $[\alpha]_D^{20} = +43.2$ (C = 1.00, $CHCl_3$), ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 2.18 (s, 3H, CH_3); 2.43–2.53 (m, 1H, H2′a); 2.86–3.00 (m, 1H, H2′b); 3.63, 3.70 (dd, 1H, H4a, $J_{4a-6} = 1.10$ and $J_{4a-4b} = 15.10$); 3.90 (d, 1H, H4b, $J_{4a-4b} = 15.10$); 4.53–4.57 (m, 2H, H5′a, H5′b); 4.79–4.84 (m, 1H, H4′, $J_{4'-5'} =$ 4.5 and $J_{4'-3'} = 1.37$); 5.53–5.58 (m, 1H, H3′); 6.33 (dd, 1H, H1′, J = 2.28 et 6.70); 7.39 et 7.45 (2d, 4H, HAr, J = 8.70); 7.61 (d, 1H, H6, $J_{6-4a} = 1.10$); 7.86–7.99 (2d, 4H, HAr, J = 8.7). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 23.6 (C-4); 24.7 (CH_3); 39.1 (C-2′); 64.1 (C-5′); 75.0 (C-3′); 84.5 (C-4′); 88.0 (C-1′); 113.9 (C-5); 127.2 to 140.5 (C-Ar); 140.6 (C-6); 164.9, 165.1 (C=O ester); 167.3 (C-2); 193.7 (C=O). I.R. KBr (ν cm^{-1}) 1723, 1636, 1269, 1233, 1092, 1015, 759. β **anomer**: $[\alpha]_D^{20} = -11.1$ (C = 1.00, $CHCl_3$), ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 2.11 (s, 3H, CH_3); 2.24–2.39 (m, 1H, H2′a); 2.67–2.78 (dd, 1H, H2′b, $J_{2'b-1'} = 5.37$ and $J_{2'b-2'a} = 14.2$); 3.62 (dd, 1H, H4a, $J_{4a-6} = 0.91$ and $J_{4a-4b} = 15.3$); 3.82 (d, 1H, H4b, $J_{4b-4a} = 15.3$); 4.51–4.56 (m, 1H, H4′); 4.65 (dd, 1H, H5′a, $J_{5'a-4'} = 4.47$ and $J_{5'a-5'b} = 12.11$); 4.76 (dd, 1H, H5′b, $J_{5'b-4'} = 3.1$ and $J_{5'a-5'b} = 12.11$); 5.58–5.61 (m, 1H, H3′); 6.42 (dd, 1H, H1′, J = 5.37 and 8.70); 7.41, 7.45 (2d, 4H, HAr, J = 2.90); 7.50 (d, 1H, H6, $J_{4a-6} = 0.91$); 7.94, 7.99 (2d, 4H, HAr, J = 8.55). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 23.3 (C-4; 24.5 (CH_3); 37.9 (C-2′); 64.5 (C-5′); 74.9 (C-3′); 82.4 (C-4′); 85.5; (C-1′); 115.3 (C-5); 127.4 to 140.3 (C-Ar); 140.3 (C-6); 165.1, 165.2 (C=O ester); 167.7 (C-2); 193.8 (C=O). MS {(CI^+, NH_4^+), $M^+18 = 567$}; (EI) M/z (%): 156 (30); 141 (29); 139 (86); 110 (35); 81 (100); 75 (21); 44 (23); 28 (23). I.R. KBr (ν cm^{-1}) 1725; 1639; 1593; 1403; 1311; 1092; 759. Anal. Calcd for $C_{25}H_{21}Cl_2NO_7S$: C, 54.55; H, 3.85; Cl, 12.88; N, 2.54; S, 5.82. Found: C,

54.33; H, 3.90; Cl, 13.26; N, 2.52; S, 4.98. (LSIMS with Cs^+, Positif in Micromasse) (Calcd. : $[M+H]^+$: 550.04947. Found: $[M+H]^+$: 550.0488

3-(3,5-Di-*O*-*p*-chlorobenzoyl-2-deoxy-α,β-D-ribofuranosyl)-4-methyl-2*H*-1,3-thiazolin-2-one (16). The protected nucleoside **15** was obtained by following a similar procedure as in the preparation of **14** from thiazolinone **11** (0.21 g, 1.83 mmol) and ribosyl chloride **13**[7] (0.87 g, 2.01 mmol). The crude product was purified by column chromatography on silica gel eluting with petroleum ether/ethyl acetate 9/1 to get **16** in 20% yield (α/β ratio 9/1). α **anomer**: $[\alpha]_D{}^{20} = +66.1$ (C = 1.00, $CHCl_3$). ^{1}H NMR ($CDCl_3$; 400 MHz) δ: 2.21 (s, 3H, CH_3); 2.92–2.98 (m, 1H, H2′a); 3.06–3.13 (m, 1H, H2′b); 4.50 (dd, 1H, H5′a, $J_{5'a-4'} = 5.1$ and $J_{5'a-5'b} = 12.04$); 4.7 (dd, 1H, H5′b, $J_{5'b-4'} = 4.74$ and $J_{5'b-5'a} = 12.04$); 4.87–4.91 (m, 1H, H4′); 5.46–5.51 (m, 1H, H3′); 5.73–5.76 (m, 1H, H4); 5.93 (t, 1H, H1′, $J_{1'-2'} = 7.22$); 7.37, 7.42 (d, 4H, HAr, J = 8.1); 7.94, 7.98 (d, 4H, HAr, J = 8.1). ^{13}C NMR ($CDCl_3$; 100 MHz) δ: 16.1 (CH_3); 34.7 (C-2′), 63.4 (C-5′), 74.3 (C-3′), 80.9 (C-4′), 84.6 (C-1′), 97.3 (C-4), 127.9 to 140.1 (C-Ar), 132.1 (C-5); 161.41, 161.43 (C=O ester), 173.2 (C-2). β **anomer**: $[\alpha]_D{}^{20} = -6.3$ (C = 1.00, $CHCl_3$).^{1}H NMR ($CDCl_3$; 400 MHz) δ: 2.21 (s, 3H, CH_3); 2.24–2.47 (m, 1H, H2′a); 3.34–3.41 (m, 1H, H2′b); 4.42 (m, 1H, H4′); 4.62 (dd, 1H, H5′a, $J_{5'a-4'} = 5.8$ and $J_{5'a-5'b} = 11.8$); 4.70 (dd, 1H, H5′b, $J_{5'b-4'} = 4.7$ and $J_{5'a-5'b} = 11.8$); 5.72–5.76 (m, 2H, H3′, H4); 5.99 (t, 1H, H1′, $J_{1'-2'a} = 7.05$); 7.40, 7.43 (2d, 4H, HAr, J = 8.55); 7.96, 7.99 (2d, 4H, HAr, J = 8.55). ^{13}C NMR ($CDCl_3$; 100 MHz) δ: 16.0 (CH_3); 34.6 (C-2′); 64.4 (C-5′); 75.5 (C-3′); 81.7 (C-4′); 84.4 (C-1′); 98.8 (C-4); 127.8 to 139.9 (C-Ar); 132.0 (C-5); 164.9, 165.4 (C=O ester); 172.7 (C-2). MS {(CI^+, $NH_4{}^+$), M+18 = 526}; (EI) M/z (%): 236 (33), 141 (43), 139 (97), 111 (30), 81 (100). Anal. Calcd for $C_{23}H_{19}Cl_2NO_9S$: C, 54.34; H, 3.77; Cl, 13.95; N, 2.76; S, 6.31. Found: C, 53.87; H, 3.81; Cl, 15.74; N, 2.41; S, 3.64.

1-(Methoxycarbonylacetylene)amide-*N*-(2-deoxy-α,β-D-ribofuranosyl) (17). A solution of **14**β (0.2 g, 0.34 mmol) in dry methanol (10 mL) was treated with sodium methoxide in methanol (0.76 mL, 0.76 mmol). The mixture was stirred for 2 h at 0°C, diluted with water (10 mL) and extracted with dichloromethane (2*30 mL). The organic layer was washed with brine (2*50 mL), dried over magnesium sulfate, filtered and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel, eluting with methanol/ethyl acetate (1/9), to give an anomeric mixture of **17** as a colorless oil in 95% yield. ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 2.80, 2.90, 2.95, 2.37 (4m, 4H, 2*H2a, 2*H2b); 3.44 (m, 4H, 2*H5a, 2*H5b); 3.66 (s, 6H, 2*CO_2CH_3); 3.70 (m, 2H, 2*H4); 4.12 (m, 2H, 2*H3); 5.58 (m, 2H, 2*H1); 7.58, 7.75 (2d, 2H, 2*NH). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 3.5 (C-2); 51.2 (CO_2CH_3); 61.4, 62.2 (C-5); 70.3, 70.7 (C-3); 81.0, 81.8 (C≡C); 84.6 (C-1); 86.1 (C-4); 97.2 (C-5); 132.3 (C-4); 174.1 (C-2); 155.7, 155.9, 181.4 (C=O). MS (EI) M/z (%) : 160 (81); 142 (35); 131 (30); 130 (25); 117 (63); 116 (44); 114 (24); 110 (20); 104 (56); 102 (96); 99 (25); 88

(43); 85 (81); 76 (82); 59 (100)–MS (CI) (NH_3): 209. I.R. KBr (ν cm^{-1}): 3426; 2922; 2852; 1700; 1636; 1565; 1420; 1123.

1-Methoxycarbamate-N-(2-deoxy-α,β-D-ribofuranosyl) (18). A solution of **15**β (0.5 g, 0.86 mmol) in dry methanol (10 mL) was treated with sodium methoxide in methanol (0.086 mL, 0.086 mmol) at room temperature until the consumption of starting material (monitored by TLC). After removal of the solvent in vacuo, the crude product was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate (7/3) then ethyl acetate/methanol (95/5), to get a mixture of anomers **18** in 60% yield. ^{1}H NMR (DMSO-d_6; 200 MHz) 1.75–1.87 (m, 1H, H2a for DIA I); 1.91–1.98 (m, 2H, H2′a, H2′b for DIA II); 2.27–2.40 (m, 1H, H2b for DIA I); 3.39–3.47 (m, 4H, H5a, H5b, H5′a, H5′b); 3.62 (s, 6H, 2(OCH_3); 3.66–3.79 (m, 2H, H4, H4′); 3.98–4.18 (m, 2H, H3, H3′); 5.40–5.58 (m, 2H, H1, H1′); 7.59, 7.75 2*(d, 1H, NH, $J_1 = 8.84$ and $J_2 = 9$). ^{13}C NMR (DMSO-d_6; 50MHz) 40.2, 40.6 (C-2); 51.2 (OCH_3); 61.4, 62.3 (C-5); 70.3, 70.5 (C-3); 81.0, 81.8 (C-4); 84.7, 86.1 (C-1); 155.7, 156.0 (C=O). MS; EI, M/z (%): {CI, NH_4^+: M+18 = 209} 160 (81); 142 (35); 131 (30); 130 (25); 117 (63); 116 (44); 114 (24); 110 (20); 104 (56); 103 (28); 102 (96); 99 (25); 98 (26); 88 (43); 85 (81); 76 (82); 73 (27); 72 (40); 70 (40); 60 (19); 59 (100); 58 (54); 57 (32); 56 (42); 45 (63); 44 (83); 43 (63); 33 (39); 31 (69); 30 (48); 29 (30).

3-(2-Deoxy-β-ribofuranosyl)-4-methyl-2*H*-1,3-thiazolin-2-one (19β). Compound **16**β (0.35 g, 0.7 mmol) dissolved in THF:H_2O mixture (v/v:7:3) (10 mL) was treated with 1M KOH (1.5 mL, 1.5 mmol). The mixture was stirred at room temperature for 3 h the solvent was removed in vacuo and the crude product was purified by flash chromatography on silica gel, eluting with ethyl acetate, to get **19**β in 80% yield. $[\alpha]_D^{20} = +2.00$ (C = 1.00, $CHCl_3$). ^{1}H NMR ($CDCl_3$; 400 MHz) δ: 2.08–2.13 (m, 1H, H2′a,); 2.17 (s, 3H, CH_3); 3.02–3.09 (m, 1H, H2′b); 3.73 (dd, 1H, H5′a, $J_{5'a-4} = 2.80$ and $J_{5'a-5'b} = 12.26$); 3.86 (dd, 1H, H5′b, $J_{5'b-4'} = 2.39$ and $J_{5'b-5'a} = 12.26$); 3.98–4.01 (m, 1H, H4′); 4.64–4.66 (m, 1H, H3′); 5.79 (s, 1H, H4); 5.85 (t, 1H, H1′, $J_{1'-2'} = 7.42$). ^{13}C NMR ($CDCl_3$; 100 MHz) δ: 16.0 (CH_3); 37.3 (C-2′); 63.0 (C-5′); 72.3 (C-3′); 85.8 (C-4′); 87.9 (C-1′); 97.3 (C-4); 132.6 (C-5); 174.3 (C-2). (LSIMS with Cs^+, Positif in Micromasse) -Calcd for $C_9H_{13}NO_4S$: $[M + H]^+ = 231.0565$. Found: $[M + H]^+ = 231.0536$.

Methyl 3-*O*-*tert*-Butyldiphenylsilyl-2-deoxy-*5*-*O*-thiocarbamoyl-α,β-D-ribofuranoside (21). Sodium hydride (60% mineral oil dispersion) (60 mg, 1.5 mmol) was added to freshly distilled tetrahydrofuran (10 mL). The solution was cooled at 0°C and **20** (450 mg, 1.16 mmol), in dry tetrahydrofuran (2 mL), was added dropwise under argon. After 15 min, carbon disulfure (0.09 mL, 1.5 mmol) was added to the mixture followed by iodomethane (0.09 mL, 1.5 mmol) after 30 min. The mixture was allowed to stir

at room temperature for 1h and the mixture was concentrated in vacuo, extracted with dichloromethane (20 mL). The organic layer was washed with brine (2*20 mL), dried over magnesium sulfate, filtered and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel, eluting with petroleum ether, to get 3-*O*-*tert*-butyldiphenylsilyl-2-deoxy-1-*O*-methyl-5-*O*-(methylthio)carbonyl-α,β-D-ribofuranoside in 95% as a yellow foamy solid. Ammonia gas was bubbled for 1 h in a solution of the 5′-carbamate ribofuranose (300 mg, 0.629 mmol) dissolved in ethanol (20 mL). Then the mixture was stirred for 12 h at room temperature and the solution was degassed, filtered on celite, concentrated in vacuo. The crude product was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate (8/2), to give **21** in 95% as a yellow foamy solid. **anomer 1**: ^{1}H NMR ($CDCl_3$; 400 MHz) δ: 1.06 (s, 9H, $C(CH_3)_3$); 1.99 (ddd, 1H, H2a, $J_{2a-2b} = 13.2$, $J_{2a-1} = 1.8$ and $J_{2a-3} = 6.8$); 2.11 (dt, 1H, H2b, $J_{2a-2b} = 13.2$, $J_{2b-1} = 5.4$ and $J_{2b-3} = 5.4$); 3.25 (s, 3H, OCH3); 4.11 (dd, 1H, H5a, $J_{5a-5b} = 11.0$ and $J_{5a-4} = 6.5$); 4.22 (m, 1H, H4); 4.32 (dd, 1H, H5b, $J_{5a-5b} = 11.0$ and $J_{5b-4} = 4.7$); 4.38 (m, 1H, H3); 5.05 (dd, 1H, H1, $J_{2a-1} = 1.8$ and $J_{2b-1} = 5.4$); 5.80 (s, 1H, NH); 6.30 (s, 1H, NH); 7.40 (m, 6H, HAr); 7.65 (m, 4H, HAr). ^{13}C NMR ($CDCl_3$; 100 MHz) δ: 19.0 ($C(CH_3)_3$); 26.9 ($C(\underline{C}H_3)_3$); 41.9 (C-2); 54.9 (OCH_3); 71.7 (C-5); 73.6 (C-3); 83.8 (C-4); 105.4 (C-1); 127.8 to 135.7 (C-Ar); 192.1 (C=S). **anomer 2**: ^{1}H NMR ($CDCl_3$; 400 MHz) δ: 1.06 (s, 9H, $C(CH_3)_3$); 1.89 (ddd, 1H, H2a, $J_{2a-2b} = 13.8$, $J_{2a-1} = 2.6$ and $J_{2a-3} = 4.9$); 2.10 (ddd, 1H, H2b, $J_{2a-2b} = 13.8$, $J_{2b-1} = 5.8$ and $J_{2b-3} = 8.1$); 3.38 (s, 3H, OCH_3); 4.12 (dd, 1H, H5a, $J_{5a-5b} = 10.2$ and $J_{5a-4} = 7.5$); 4.12 (m, 2H, H5b, H3, $J_{5a-5b} = 11.4$ and $J_{5b-4} = 4.7$); 4.21 (m, 1H, H4); 4.44 (dd, 1H, H5b, $J_{5a-5b} = 11.4$ and $J_{5b-4} = 3.1$); 4.90 (dd, 1H, H1, $J_{2a-1} = 2.6$ and J_{2b-1}=5.8); 5.90 (s, 1H, NH); 6.40 (s, 1H, NH); 7.40 (m, 6H, HAr); 7.68 (m, 4H, HAr). ^{13}C NMR ($CDCl_3$; 100 MHz) δ: 19.1 ($\underline{C}(CH_3)_3$); 26.9 ($C(\underline{C}H_3)_3$); 41.5 (C-2); 55.1 (OCH_3); 70.3 (C-5); 72.7 (C-3); 81.4 (C-4); 104.6 (C-1); 127.8 to 135.8 (C-Ar); 192.1 (C=S).

Methyl 3-*O*-*tert*-Butyldiphenylsilyl-2-deoxy-5-*O*-[(4-dimethylamino)-1-thia-3-aza-1,3-butadienyl]-α,β-D-ribofuranoside (22a). To a solution of **21** (0.3 g, 0.67 mmol) in dry dichloromethane (10 mL) was added *N,N*-dimethylformamide dimethyl acetal (0.1 mL, 0.74 mmol) dropwise. The solution was stirred at room temperature for 1 h and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate (4/6), to get **22a** in 95% as a yellow syrup. MS (EI) M/z (%): 213 (32); 199 (58); 183 (27); 116 (29); 99 (100); 81 (61). MS (CI) (NH_3) [M+H$^+$] = 501−I.R. KBr (ν cm^{-1}): 3071; 3047; 2932; 2857; 1630; 1280; 1229; 1114; 706; 506. **anomer 1**: ^{1}H NMR ($CDCl_3$; 400 MHz) δ: 1.05 (s, 9H, $C(CH_3)_3$); 1.98 (ddd, 1H, H2a, $J_{2a-2b} = 13.0$, $J_{2a-1} = 2.05$ and $J_{2a-3} = 6.05$); 2.05 (dt, 1H, H2b, $J_{2a-2b} = 13.0$, $J_{2b-1} = 5.2$ and $J_{2b-3} = 5.2$); 3.11

(s, 3H, NCH_3); 3.19 (s, 3H, NCH_3); 3.26 (s, 3H, OCH3); 4.34, 4.42 (2*m, 2*2H, H3, H4, H5a, H5b); 5.05 (dd, 1H, H1, $J_{2a-1} = 2.05$ and $J_{2b-1} = 5.2$); 7.38 (m, 6H, HAr); 7.65 (m, 4H, HAr); 8.73 (s, 1H, H4′)–^{13}C NMR ($CDCl_3$; 100 MHz) δ: 19.1 ($\underline{C}(CH_3)_3$); 26.9 ($C(\underline{C}H_3)_3$); 36.3 (NCH_3); 41.9 (NCH_3); 42.1 (C-2); 55.0 (OCH_3); 72.5 (C-5); 74.2 (C-3); 84.1 (C-4); 105.5 (C-1); 127.8 to 135.9 (C-Ar); 164.0 (C-4′); 205.0 (C=S). **anomer 2**: ^{1}H NMR ($CDCl_3$; 400 MHz) δ 1.87 (ddd, 1H, H2a, $J_{2a-2b} = 13.7$, $J_{2a-1} = 2.3$ and $J_{2a-3} = 4.5$); 2.10 (ddd, 1H, H2b, $J_{2a-2b} = 13.7$, $J_{2b-1} = 5.7$ and $J_{2b-3} = 8.0$); 3.09 (s, 3H, NCH_3); 3.19 (s, 3H, NCH_3); 3.38 (s, 3H, OCH_3); 4.21 (m, 1H, H3); 4.22 (dd, 1H, H5a, $J_{5a-5b} = 11.8$ and $J_{5a-4} = 6.3$); 4.34 (m, 2H, H4); 4.45 (dd, 1H, H5b, $J_{5a-5b} = 11.8$ and $J_{5b-4} = 2.7$); 4.93 (dd, 1H, H1, $J_{2a-1} = 2.35$ and $J_{2b-1} = 5.7$); 7.35 (m, 6H, HAr); 7.64 (m, 4H, HAr); 8.72 (s, 1H, H4′). ^{13}C NMR ($CDCl_3$; 100 MHz) δ: 19.2 ($\underline{C}(CH_3)_3$); 27.0 ($C(\underline{C}H_3)_3$); 36.3 (NCH_3); 41.6 (C-2); 41.9 (NCH_3); 55.1 (OCH_3); 70.9 (C-5); 73.3 (C-3); 81.9 (C-4); 104.8 (C-1); 127.7 to 135.9 (C-Ar); 163.9 (C-4′); 205.1 (C=S).

Methyl 3-*O*-*tert*-Butyldiphenylsilyl-2-deoxy-5-*O*-[(4-dimethylamino)-1-thia-3-aza-1,3-pentadienyl]-α,β-D-ribofuranoside (22b). To a solution of **21** (0.35 g, 0.78 mmol) in dry dichloromethane (10 mL) was added *N,N*-dimethylacetamide dimethyl acetal (0.23 mL, 1.56 mmol) dropwise. The solution was stirred at reflux for 5 h, cooled, and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate (4/6), to get **22b** in 95% as a yellow syrup. MS (EI) M/z (%): 514; 311 (28); 254 (22); 213 (27); 199 (51); 197 (26); 183 (40); 181 (37); 163 (32); 135 (51); 129 (39); 113 (100); 91 (28); 87 (26); 81 (22); 72 (23); 71 (26) – I.R. KBr (ν cm^{-1}): 3071; 2956; 2932; 2344; 1588; 1370; 1109; 1048; 706; 506. -Anal. Calcd for $C_{27}H_{38}N_2O_4SSi$: C, 63.00; H, 7.44; N, 5.44. Found: C, 62.79; H, 7.51; N, 5.44. **anomer 1**: ^{1}H NMR ($CDCl_3$; 400 MHz) δ: 1.06 (s, 9H, $C(CH_3)_3$); 1.93 (ddd, 1H, H2a, $J_{2a-2b} = 13.3$, $J_{2a-1} = 2.2$ and $J_{2a-3} = 6.6$); 2.04 (dt, 1H, H2b, $J_{2a-2b} = 13.3$ and $J_{2b-1} = 5.4$); 2.32 (s, 3H, C-4-CH_3); 3.06 (s, 3H, NCH_3); 3.08 (s, 3H, NCH_3); 3.26 (s, 3H, OCH_3); 4.13 (dd, 1H, H5a, $J_{5a-5b} = 11.4$ and $J_{5a-4} = 7.5$); 4.28 (dd, 1H, H5b, $J_{5a-5b} = 11.4$ and $J_{5b-4} = 4.5$); 4.35 (m, 1H, H4); 4.43 (m, 1H, H3); 5.05 (dd, 1H, H1, $J_{2a-1} = 2.2$ and $J_{2b-1} = 5.2$); 7.38 (m, 6H, HAr); 7.66 (m, 4H, HAr). ^{13}C NMR ($CDCl_3$; 100 MHz) δ: 17.7 (C-5′); 19.1 ($\underline{C}(CH_3)$); 27.0 ($C(\underline{C}H_3)$); 38.7 (NCH_3); 38.9 (NCH_3); 42.1 (C-2); 55.0 (OCH_3); 72.2 (C-5); 74.2 (C-3); 84.4 (C-4); 105.5 (C-1); 127.8 to 135.9 (C-Ar); 165.1 (C-4′); 196.7 (C=S). **anomer 2**: ^{1}H NMR ($CDCl_3$; 400 MHz) δ: 1.06 (s, 9H, $C(CH_3)_3$); 1.85 (m, 1H, H2a); 2.07 (m, 1H, H2b); 2.34 (s, 3H, C-4-CH_3); 3.06 (s, 3H, NCH_3); 3.08 (s, 3H, NCH_3); 3.37 (s, 3H, OCH_3); 4.11 (dd, 1H, H5a, $J_{5a-5b} = 11.7$ and $J_{5a-4} = 5.7$); 4.22 (m, 1H, H3); 4.27 (m, 1H, H4); 4.38 (dd, 1H, H5b, $J_{5a-5b} = 11.7$ and $J_{5b-4} = 2.5$); 4.92 (m, 1H, H1); 7.39 (m, 6H, HAr); 7.65 (m, 4H, HAr); 8.72 (s, 1H, H4′). ^{13}C NMR ($CDCl_3$; 100 MHz) δ: 17.7 (C-5′); 19.1 ($\underline{C}(CH_3)_3$); 27.0 ($C(\underline{C}H_3)_3$); 38.7

(NCH_3); 38.9 (NCH_3); 41.6 (C-2); 55.1 (OCH_3); 70.4 (C-5); 73.1 (C-3); 82.1 (C-4); 104.8 (C-1); 127.7 to 135.8 (C-Ar); 165.1 (C-4′); 196.7 (C=S).

Methyl 3-*O*-*tert*-Butyldiphenylsilyl-2-deoxy-5-*O*-[2-(6-methoxycarbonyl)-4-oxo-4*H*-1,3-thiazine-4-onyl]-α,β-D-ribofuranoside (23). To a solution of **21** (0.2 g, 0.45 mmol) in methanol (2 mL) was added dimethyl acetylenedicarboxylate (0.11 mL, 0.90 mmol) dropwise. The mixture was stirred at room temperature for 24 h and diluted with dichloromethane (20 mL). The organic layer was washed with brine (3*50 mL), dried over magnesium sulfate, filtered and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate (9/1), to give **23** in 70% as a white foamy solid. MS (EI) M/z (%) : 498 (47); 268 (27); 213 (80); 199 (25); 183 (59); 135 (31); 81 (100) MS (CI) (NH_3) [$M+H^+$] = 556 [$M+NH_4^+$] = 578. **anomer 1**: ^{1}H NMR ($CDCl_3$; 400 MHz) δ: 1.06 (s, 9H, $C(CH_3)_3$); 2.07 (ddd, 1H, H2a, $J_{2a-2b} = 13.1$, $J_{2a-1} = 1.4$ and $J_{2a-3} = 6.8$); 2.16 (ddd, 1H, H2b, $J_{2a-2b} = 13.1$, $J_{2b-1} = 5.2$ and $J_{2b-3} = 6.4$); 3.22 (s, 3H, OCH_3); 3.86 (s, 3H, CO_2CH_3); 4.26 (m, 1H, H4); 4.28 (dd, 1H, H5a, $J_{5a-5b} = 10.1$ and $J_{5b-4} = 6.0$); 4.36 (dd, 1H, H5b, $J_{5a-5b} = 10.1$ and $J_{5b-4} = 4.1$); 4.45 (m, 1H, H3); 5.05 (dd, 1H, H1, $J_{2a-1} = 1.4$ and $J_{2b-1} = 5.2$); 7.02 (s, 1H, H5′); 7.40 (m, 6H, HAr); 7.63 (m, 4H, HAr). ^{13}C NMR ($CDCl_3$; 100 MHz) δ: 19.1 ($\underline{C}(CH_3)$); 27.0 ($C(\underline{C}H_3)$); 42.1 (C-2); 53.0 ($CO_2\underline{C}H_3$); 55.0 (OCH_3); 73.2 (C-3); 74.8 (C-5); 83.3 (C-4); 105.5 (C-1); 120.2 (C-5′); 128.0 to 135.8 (C-Ar); 146.6 (C-6′); 166.3 ($\underline{C}O_2CH_3$); 177.9 (C-4′); 190.0 (C-2′). **anomer 2**: ^{1}H NMR ($CDCl_3$; 400 MHz) δ: 1.06 (s, 9H, $C(CH_3)_3$); 1.98 (ddd, 1H, H2a, $J_{2a-2b} = 13.7$, $J_{2a-1} = 2.6$ and $J_{2a-3} = 4.6$); 2.24 (m, 1H, H2b); 3.39 (s, 3H, OCH_3); 3.87 (s, 3H, CO_2CH_3); 4.21 (m, 3H, H3, H4, H5a); 4.54 (dd, 1H, H5b, $J_{5a-5b} = 11.3$ and $J_{5b-4} = 1.5$); 4.93 (dd, 1H, H1, $J_{2a-1} = 2.6$ and $J_{2b-1} = 5.7$); 7.02 (s, 1H, H5′); 7.40 (m, 6H, HAr); 7.63 (m, 4H, HAr). ^{13}C NMR ($CDCl_3$; 100 MHz) δ: 19.0 ($\underline{C}(CH_3)_3$); 26.8 ($C(\underline{C}H_3)_3$); 41.5 (C-2); 52.7 ($CO_2\underline{C}H_3$); 55.1 (OCH_3); 72.0 (C-3); 72.9 (C-5); 80.6 (C-4); 104.5 (C-1); 119.5 (C-5′); 127.8 to 135.7 (C-Ar); 146.4 (C-6′); 166.0 ($\underline{C}O_2CH_3$); 177.5 (C-4′); 189.8 (C-2′).

Methyl 3-*O*-*tert*-Butyldiphenylsilyl-2-deoxy-5-*O*-[2-5-acetyl-6*H*-1,3-thiazin-2-yl]-α,β-ribofuranoside (24). A solution of **22a** (0.1 g, 0.2 mmol) in methyl vinyl ketone (2 mL) was heated at reflux for 2 h. The mixture was diluted with dichloromethane (10 mL) and washed with brine (2*20 mL). After extraction with dichloromethane, the organic layer was dried over magnesium sulfate, filtered and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate (8/2), to get **24** in 80% as a white foamy solid. ^{1}H NMR ($CDCl_3$; 400 MHz) δ: 1.06 (s, 9H, $C(CH_3)_3$); 1.91 (ddd, 1H, H2a, $J_{2a-2b} = 13.7$, $J_{2a-1} = 2.5$ and $J_{2a-3} = 7.4$); 2.16 (m, 1H, H2b); 2.37 (s, 3H, CO_2CH_3); 3.39 (s, 3H, OCH_3); 3.68 (s, 2H, H6′); 4.08 (dd, 1H, H5a,

$J_{5a-5b} = 11.8$ and $J_{5a-4} = 4.4$); 4.20 (m, 2H, H3, H4); 4.38 (dd, 1H, H5b, $J_{5a-5b} = 11.8$ and $J_{5b-4} = 2.5$); 4.93 (dd, 1H, H1, $J_{2a-1} = 2.5$ and $J_{2b-1} = 5.7$); 7.38 (m, 6H, HAr); 7.55 (s, 1H, H4′); 7.63 (m, 4H, HAr). ^{13}C NMR ($CDCl_3$; 100 MHz) δ: 19.3 ($\underline{C}(CH_3)_3$); 23.1 (C-6′); 25.4 ($CO\underline{C}H_3$); 27.0 ($C(\underline{C}H_3)_3$); 41.7 (C-2); 55.4 (OCH_3); 68.0 (C-5); 72.6 (C-3); 81.4 (C-4); 104.8 (C-1); 115.7 (C-5′); 127.9 to 136.0 (C-Ar); 147.9 (C-6′); 167.7 (C-2′); 195.9 ($COCH_3$). MS (EI) M/z (%): 213 (24); 199 (100); 183 (23); 81 (33). MS (CI) (NH_3) $[M+H^+] = 526$. I.R. KBr (ν cm^{-1}): 2931; 2856; 1698; 1111; 739; 502.

Methyl 3-*O*-*tert*-Butyldiphenylsilyl-2-deoxy-5-*O*-[2-(4-methyl)-1,3-thiazol -2-yl]-α,β-D-ribofuranoside (25). Sodium hydride (60% mineral oil dispersion) (96 mg, 2.41 mmol) was added to a solution of trimethyl sulfonium iodide (530 mg, 2.41 mmol) in freshly distilled dimethylsulfoxide (15 mL). After stirring at room temperature for 30 min **22b** (620 mg, 1.2 mmol) was added. Stirring was continued for 12 h. The mixture was diluted with ethyl acetate (60 mL) and washed with water (3*60 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated in vacuo. The thiazoline intermediate obtained as a white foamy solid (700 mg, 1.32 mmol) was dissolved in dry toluene (20 mL) and treated with iodomethane (0.25 mL, 3.96 mmol). The mixture was stirred under argon at reflux for 2 h. The solution was filtered on celite, concentrated under vacuo. Dichloromethane (30 mL) was added and the solution was washed with brine (2*30 mL). After extraction, the organic layer was dried over magnesium sulfate, filtered and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate (9/1), to get **25** in 50% as a colorless syrup. MS (CI) (NH_3) $[M+H^+] = 484$. I.R. KBr (ν cm^{-1}) : 3071; 3049; 2952; 2857; 1517; 1305; 112; 703. **anomer 1**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.06 (s, 9H, $C(CH_3)_3$); 1.91 (ddd, 1H, H2a, $J_{2a-2b} = 13.5$, $J_{2a-1} = 2.4$, $J_{2a-3} = 4.4$); 2.15 (ddd, 1H, H2b, $J_{2a-2b} = 13.5$, $J_{2b-1} = 5.7$, $J_{2b-3} = 7.7$); 2.23 (s, 3H, C-4′-CH_3); 3.39 (s, 3H, OCH_3); 4.11 (dd, 1H, H5a, $J_{5a-5b} = 11.2$, $J_{5a-4} = 4.4$); 4.25 (m, 1H, H4); 4.28 (m, 1H, H3); 4.36 (dd, 1H, H5b, $J_{5a-5b} = 11.2$, $J_{5b-4} = 2.6$); 4.94 (dd, 1H, H1, $J_{2a-1} = 2.4$, $J_{2b-1} = 5.7$); 6.17 (s, 1H, H5′); 7.35 (m, 6H, HAr); 7.64 (m, 4H, HAr). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 17.2 (C-4′-$\underline{C}H_3$); 19.2 ($\underline{C}(CH_3)_3$); 27.0 ($C(\underline{C}H_3)_3$); 41.8 (C-2); 55.3 (C-Ar-$O\underline{C}H_3$); 70.0 (C-5); 72.4 (C-3); 81.9 (C-4); 104.8 (C-1); 105.1 (C-5′); 127.8 to 136.0 (C-Ar); 146.7 (C-4′); 173.0 (C-2′). **anomer 2**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.06 (s, 9H, $C(CH_3)_3$); 1.99 (ddd, 1H, H2a, $J_{2a-2b} = 13.2$, $J_{2a-1} = 2.0$, $J_{2a-3} = 6.7$); 2.10 (dt, 1H, H2b, $J_{2a-2b} = 13.2$, $^3J = 5$); 2.22 (s, 3H, C-4′-CH_3); 3.24 (s, 3H, OCH_3); 4.13 (dd, 1H, H5a, $J_{5a-5b} = 10.8$, $J_{5a-4} = 6.7$); 4.18 (dd, 1H, H5b, $J_{5a-5b} = 10.8$, $J_{5b-4} = 4.7$); 4.31 (m, 1H, H4); 4.47 (m, 1H, H3); 5.07 (dd, 1H, H1, $J_{2a-1} = 2.0$, $J_{2b-1} = 5.7$); 6.18 (s, 1H, H5′); 7.36 (m, 6H, HAr); 7.65 (m, 4H, HAr).^{13}C NMR ($CDCl_3$, 100 MHz) δ: 17.9 (C-4′-$\underline{C}H_3$); 19.2 ($\underline{C}(CH_3)_3$); 27.0 ($C(\underline{C}H_3)_3$); 42.1 (C-2);

55.1 (C-Ar-O<u>C</u>H$_3$); 71.9 (C-5); 73.8 (C-3); 84.2 (C-4); 105.1 (C-5′); 105.6 (C-1′); 127.9 to 135.9 (C-Ar); 146.7 (C-4′); 173.7 (C-2′).

3-[(3-*O*-*tert*-Butyldiphenylsilyl)-2′-deoxy-β-D-ribofuranosyl]-4-methyl-1,3-thiazolin-2-one (26). To a solution of **25** (0.150 g, 0.31 mmol) in freshly distilled acetonitrile (30 mL), was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.06 mL, 0.31 mmol) dropwise at −20°C under argon atmosphere. After 1 h of stirring, an additional amount of *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.06 mL, 0.31 mmol) was added at 0°C before the addition of *tert*-butyldiphenylsilyl chloride (0.16 mL, 0.62 mmol). The mixture was stirred for another 6 h. After adding saturated aqueous solution of sodium hydrogenocarbonate (3 mL), the stirring was continued for 12h. The solution was diluted with ammonium chloride (60 mL), then extracted with dichloromethane (2*50 mL). The organic layers were washed with water (2*50 mL), dried over magnesium sulfate, filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel eluting with ethyl acetate petroleum ether (2/8), to get **26** in 20% yield. ^{1}H NMR ($CDCl_3$; 400 MHz) δ: 1.10 (s, 9H, C(C<u>H</u>$_3$)$_3$); 1.96 (dd, 1H, H2′a, $J_{2'a-2'b}=13.1$, $J_{2'a-1'}=5.8$); 2.17 (s, 3H, C4′-C<u>H</u>$_3$); 2.97 (ddd, 1H, H2′b, $J_{2'a-2'b}=13.1$, $J_{2'b-1'}=9.5$, $J_{2'b-3'}=5.7$); 3.19 (m, 1H, H5′a); 3.63 (dd, 1H, H5′b, $J_{5'a-5'b}=12.4$, $J_{5'b-4'}=2.6$); 3.90 (m, 1H, OH); 4.02 (m, 1H, H4′); 4.64 (m, 1H, H3′); 5.75 (s, 1H, H5); 5.87 (dd, 1H, H1′, $J_{2'a-1'}=5.8$, $J_{2'b-1'}=9.5$); 7.40 (m, 6H, HAr); 7.64 (m, 4H, HAr). ^{13}C NMR ($CDCl_3$; 100MHz) δ: 15.9 (C4′-<u>C</u>H$_3$); 19.0 (<u>C</u>(CH$_3$)$_3$); 26.9 (C(<u>C</u>H$_3$)$_3$); 37.5 (C-2′); 63.0 (C-5′); 74.7 (C-3′); 86.3 (C-1′); 89.1 (C-4′); 97.2 (C-5); 127.8 to 135.7 (C-Ar, C-4); 173.8 (C-2). MS (CI) (NH_3) $[M+H^+]=470$; $[M+NH_4^+]=487$.

3-(5-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-α,β-D-ribofuranosyl)-6-methoxycarbonyl-4*H*-1,3-thiazin-2,4-dione (29). To a solution of sodium hydride (60% mineral oil dispersion) (0.1 g, 2.57 mmol) in dry acetonitrile (5 mL), at 0°C under argon, was added thiazindione **3** (0.33 g, 2.12 mmol). The mixture was stirred for 15 min and freshly prepared ribofuranosyl chloride **28**[8] (0.61 g, 1.37 mmol) was added. After 30 min, the mixture was allowed to warm to room temperature and stirred for another 15 h.p

Water (100 mL) and dichloromethane (2*100 mL) were added. After extraction, the organic layer was washed with brine, dried over magnesium sulfate, filtered and evaporated in vacuo. The crude product was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate (8/2), to get an anomeric mixture of **29** in 54% yield (α, β ratio = 1/1). ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 1.05, 1.08 2*(s, 9H, tBu); 1.19, 1.45 2*(s, 3H, CMe$_2$); 1.33, 1.55 2*(s, 3H, CMe$_2$); 3.67–3.83 (m, 2*2H, H5′a, H5′b); 3.83, 3.84 2*(s, 3H, OCH$_3$); 4.20–4.25, 4.65–4.66 (m, 2*1H, H4′); 4.84–4.98 (m, 3H, 2*H2′, H3′); 5.07–5.11 (dd, 1H, H3′, J = 1.75 and 6.26); 5.93, 6.30 2*(d, 1H, H1′, $J_{1'-2'}=1.8$ and 4.9); 6.95, 7.00 2*(s, 1H, H5); 7.35–7.41,

7.63–7.69 (m, 20H, HAr). ^{13}C NMR ($CDCl_3$; 100 MHz) δ: 19.1, 19.2 ($\underline{C}(CH_3)_3$); 24.3, 25.3 ($\underline{Me}_2C$); 25.7, 27.2 ($\underline{Me}_2C$); 26.8 ($C(\underline{C}H_3)_3$); 52.7, 52.8 (OCH_3); 64.1, 65.1 (C-5′); 80.1, 81.8 (C-2′); 84.9, 88.1 (C-4′); 81.6, 82.7 (C-3′); 87.3, 88.6 (C-1′); 114.0, 114.9 ($Me_2\underline{C}$); 118.3, 119.4 (C-5); 127.5 to 135.6 (C-Ar); 140.0, 140.7 (C-6); 163.7, 163.8 (C-4); 165.5, 165.8 (C=O ester); 167.0, 168.0 (C-2). MS {(Cl^+, NH_4^+), M+18 = 615}; (EI) M/z (%): 295 (29); 270 (100); 217 (21); 213 (16); 212 (40); 199 (31); 184 (46); 167 (40); 135 (30); 85 (20); 59 (15); 57 (20); 43 (25).

5-Acetyl-3-(5-*O*-*tert*-butyldiphenylsilyl-2,3-O-isopropylidene-α,β-ribofuranosyl)-3,6-dihydro-2*H*-1,3-thiazin-2-one (30). An anomeric mixture of **30** was obtained by following a similar experimental procedure as mentioned for **29**, starting from thiazinone **6**, in 50% yield (α/β ratio = 1/3). ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 1.12 (s, 9H, tBu); 1.35 (s, 3H, CMe); 1.51 (s, 3H, CMe); 2.35 (s, 3H, CH_3C=O); 3.73 (dd, 1H, H5′a, $J_{5'a-4'} = 2.50$ and $J_{5'a-5'b} = 11.30$); 3.85 (d, 2H, H4, J = 2.22); 3.89 (dd, 1H, H5′b, $J_{5'b-4'} = 2.80$ and $J_{5'a-5'b} = 11.30$); 4.36 (m, 1H, H4′); 4.82 (d, 1H, H3′, $J_{3'-2'} = 6.10$); 4.94 (dd, 1H, H2′, $J_{2'-1'} = 4.30$ and $J_{3'-2'} = 6.10$); 6.5 (d, 1H, H1′, $J_{1'-2'} = 4.3$); 7.42–7.46 (m, 5H, HAr); 7.65–7.68 (m, 6H, H6, HAr). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 19.0 ($\underline{C}(\underline{C}H_3)_3$); 23.2 (C-4); 23.8 ($\underline{C}H_3$-C); 24.8 ($\underline{C}H_3$-C=O); 26.0 ($\underline{C}H_3$-C); 26.8 ($C(\underline{C}H_3)_3$); 65.9 (C-5′); 79.5 (C-2′); 81.7 (C-3′); 83.2 (C-4′); 87.3 (C-1′); 112.4 ($Me_2\underline{C}$); 112.8 (C-5); 127.6 to 135.6 (C-Ar); 139.1 (C-6); 167.0 (C-2); 194.4 (C=O). MS {(CI^+, NH_4^+ M+18) = 585}; (EI) M/z (%) : 511 (30); 510 (81); 392 (19); 353 (17); 339 (26); 338 (100); 296 (22); 295 (79); 253 (19); 251 (18); 241 (26); 223 (26); 217 (33); 197 (37); 182 (84); 181 (25); 176 (17); 163 (74); 161 (24); 139 (28); 138 (68); 135 (71); 121 (16); 115 (25); 110 (26); 105 (21); 91 (14); 77 (16); 43 (39). Anal. Calcd for $C_{30}H_{37}NO_6SSi$: C, 63.46; H, 6.57; N, 2.47; S, 5.67; Si, 4.95. Found: C, 63.21; H, 6.53; N, 2.42; S, 5.79; Si, 4.70.

3-(5-*O*-*tert*-Butyldiphenylsilyl-2,3-O-isopropylidene-α,β-ribofuranosyl)-4-methyl-2*H*-1,3-thiazolin-2-one (31). Compound **31** was obtained following a similar experimental procedure as mentioned for **29** starting from thiazolinone **11** in 47% yield. Anomers **31**α and **31**β were isolated by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether (3/7), in 1/2 α/βratio. α **anomer**: $[\alpha]_D^{20} = +52.9$ (C = 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$; 200 MHz) δ (delta) = 1.07 (s, 9H, tBu); 1.38 (s, 3H, CMe_2); 1.59 (s, 3H, CMe_2); 2.27 (d, 3H, CH_3, $J_{CH_3\text{-}CH} = 1.06$); 3.77 (dd, 1H, H5′a, $J_{5'a-4'} = 2.75$ and $J_{5'a-5'b} = 11.29$); 3.86 (dd, 1H, H5′b, $J_{5'b-4'} = 3.20$ and $J_{5'b-5'a} = 11.29$); 4.43-4.46 (m, 1H, H4′); 4.83 (dd, 1H, H3′, J = 1.83 and $J_{2'-3'} = 6.56$); 4.93 (dd, 1H, H2′, $J_{2'-1'} = 4.27$ and $J_{3'-2'} = 6.56$); 6.24 (q, 1H, H4, J = 1.06); 6.42 (d, 1H, H1′, $J_{1'-2'} = 4.27$); 7.38–7.41 and 7.64–7.70 (m, 10H, HAr). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 17.7 ($\underline{C}(CH_3)_3$); 19.2 (CH_3); 25.7, 25.9 ($C(CH_3)_2$); 26.8 ($C(CH_3)_3$); 64.2 (C-5′); 80.5 (C-3′); 80.8 (C-2′); 83.6 (C-4′); 101.7 (C-1′); 105.4 (C-4); 114.9 ($\underline{C}Me_2$); 127.6 to 135.6 (C-Ar); 146.9 (C-5);

171.8 (C-2). MS {CI^+, NH_4^+, [M + H] = 526}; (EI) M/z (%): 469 (24); 468 (74); 296 (71); 295 (71); 275 (23); 221 (42); 217 (27); 199 (46); 198 (30)197 (47); 183 (21); 181 (20); 163 (31); 161 (81); 140 (19); 135 (100); 129 (24); 116 (18); 115 (25); 91 (24); 77 (20); 57 (25); 43 (35); 41 (18). β **anomer**: $[\alpha]_D^{20} = -4.2$ (C = 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 1.10 (s, 9H, tBu); 1.31 (s, 3H); 1.48 (s, 3H); 2.31 (d, 3H, J = 1.2); 3.72 (dd, 1H, H5′a, $J_{5'a-4'} = 2.8$ and $J_{5'a-5'b} = 11.1$); 3.84 (dd, 1H, H5′b, $J_{5'b-4'} = 3.3$); 4.28 (t, 1H, H4′); 4.83 (dd, 1H, H3′, J = 0.9 and $J_{3'-2'} = 6.2$); 4.93 (dd, 1H, H2′, $J_{2'-1'} = 4.5$ and $J_{2'-3'} = 6.2$); 5.63 (q, 1H, H-C4, J = 1.2); 6.40 (d, 1H, H1′, $J_{1'-2'} = 4.5$); 7.39–7.69 (m, 10H, HAr). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 17.5 ($\underline{C}(CH_3)_3$; 19.2 ($\underline{C}H_3$); 23.7 ($\underline{Me}_2C$); 25.4 ($\underline{Me}_2C$); 26.8 ($C(\underline{C}H_3)_3$); 65.7(C-5′); 79.8 (C-2′); 82.9 (C-3′); 89.3 (C-4′); 96.0 (C-1′); 113.2 ($Me_2\underline{C}$); 127.8 to 135.6 (C-Ar); 146.9 (C-5), 172.6 (C-2). MS {CI^+, NH_4^+, [M + H] = 526}; (EI) M/z (%): 469 (33); 468 (100); 296 (33); 295 (49); 275 (20); 221 (31); 217 (26); 199 (41); 198 (14); 197 (38); 183 (21); 181 (21); 163 (28); 161 (77); 140 (46); 135 (94); 129 (23); 115 (28); 91 (31); 77 (18). Anal. Calcd for $C_{28}H_{35}NO_5SSi$: C, 63.97; H, 6.71; N, 2.66; S, 6.10; Si, 6.34. Found: C, 63.75; H, 6.72; N, 2.37; S, 5.94; Si, 6.35.

3-(2,3-*O*-Isopropylidene-α,β-D-ribofuranosyl)-6-methoxycarbonyl-4*H*-1,3-thiazin-2,4-dione (32). A solution of **30** (1.1 g, 1.93 mmol) in methanol (10 mL) was treated with *p*-toluene sulfonic acid (0.73 g, 3.86 mmol). The mixture was stirred at room temperature for 6 h. Water (100 mL) and dichloromethane (2*100 mL) were added. After extraction, the organic layer was washed with brine (100 mL), dried over magnesium sulfate, filtered and concentrated. The crude product was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate (1/1), to get **32**α and **32**β in 60% yield (α/β ratio = 1/1). α **anomer**: $[\alpha]_D^{20} = +39.4$ (C = 1.00, $CHCl_3$). ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 1.32 and 1.45 (2s, 2x3H, CMe_2); 2.25 (1H, OH); 3.67–3.78 (m, 2H, H5′a, H5′b); 3.86 (s, 1H, 3H, OCH_3); 4.71–4.76 (m, 1H, H4′); 4.82–4.91 (m, 2H, H2′, H3′); 6.20–6.23 (m, 1H, H1′); 7.00 (s, 1H, H5). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 24.7 and 25.6 ($C(\underline{C}H_3)_2$); 52.9 ($O\underline{C}H_3$); 63.1 (C-5′); 80.3 (C-2′); 81.5 (C-3′); 85.8 (C-4′); 87.8 (C-1′); 115.8 ($\underline{C}(CH_3)_2$); 118.7 (C-5); 140.7 (C-6); 163.9 (C-4); 165.9 (C=O ester); 167.5 (C-2). β **anomer**: $[\alpha]_D^{20} = -39.2$ (C = 1.00, $CHCl_3$). ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 1.28 and 1.51 (2s, 2x3H, CMe_2); 2.51 (1H, OH); 3.61–3.80 (m, 5H, H5′a, H5′b and OCH_3); 4.16–4.21 (m, 1H, H4′); 4.87 (dd, 1H, H3′, $J_{3'-4'} = 3.52$, $J_{3'-2'} = 6.4$); 5.05 (dd, 1H, H2′, $J_{2'-3'} = 6.4$, $J_{2'-1'} = 3.36$); 5.86 (d, 1H, H1′, $J_{1'-2'} = 3.36$); 6.98 (s, 1H, H5). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 25.5 and 27.4 ($C(\underline{C}H_3)_2$); 53.1 ($O\underline{C}H_3$); 63.0 (C-5′); 80.8 (C-2′); 82.0 (C-3′); 86.7 (C-4′); 88.1 (C-1′); 114.6 ($\underline{C}(CH_3)_2$); 120.1 (C-5); 139.7 (C-6); 164.2 (C-4); 165.6 (C=O ester); 168.7 (C-2). MS {CI^+, NH_4^+, M+18 = 377}; M/z (%) : 344 (65); 116 (15); 86 (23); 85 (52); 71 (17); 69 (24); 68 (32); 59 (77); 57 (39); 43 (100); 41 (29); 31 (34); 29 (27). (LSIMS with Cs^+, Positif in Micromasse)-Calcd for $C_{14}H_{17}NO_8S$: $[M + H]^+ = 359.0753$ Found: $[M + H]^+ = 360.0752$.

6-Methoxycarbonyl-3-(α,β-D-ribofuranosyl)-4*H*-1,3-thiazin-2,4-dione (33). Dowex 50X2-200 (0.31 g, 0.86 mmol), previously washed twice with methanol, was added to the α or β anomer of **32** (88 mg, 0.245 mmol) in solution in methanol (5 mL). The mixture was stirred at room temperature for 15h, filtered and the resin was washed twice with methanol. The solution was evaporated in vacuo and the crude product was purified by preparative TLC, eluting with ethyl acetate, to get the ribosyls **33**α or **33**β in 65% overall yield. α **anomer**: $[\alpha]_D^{20} = +25{,}5$ (C = 1, MeOH). ^{1}H NMR (CD_3OD; 200 MHz) δ: 3.63–3.67 (m, 2H, H5′a and H5′b); 3.84 (s, 3H, OCH_3); 4.58–4.63 (m, 2H, H4′, H3′); 4.71–4.76 (m, 1H, H2′); 6.19 (d, 1H, H1′, $J_{1'-2'} = 5.34$); 6.96 (s, 1H, H5). ^{13}C NMR (CD_3OD; 50 MHz) δ: 45.3 (C-5′); 55.1 (OCH_3); 63.6 (C-2′); 64.1 (C-3′); 77.9 (C-4′); 80.9 (C-1′); 112.0 (C-5); 133.2 (C-6); 155.3 (C-4); 159.0 (C=O ester); 161.7 (C-2). MS {CI, NH_4^+, M+18 = 337}, (EI), M/z (%) : 246 (15); 189 (15); 188 (46); 160 (15); 133 (40); 132 (44); 117 (26); 116 (23); 114 (17); 101 (15); 86 (15); 85 (83); 74 (18); 73 (100); 60 (32); 59 (32); 58 (21); 57 (71); 55 (19); 45 (26); 43 (23); 31 (33); 29 (31). β **anomer**: $[\alpha]_D^{20} = -35{,}3$ (C = 1, MeOH). ^{1}H NMR (CD_3OD; 400 MHz) δ: 3.65 (dd, 1H, H5′a, $J_{5'a-4'} = 5.8$ and $J_{5'a-5'b} = 12$); 3.77 (dd, 1H, H5′b, $J_{5'b-4'} = 3.5$ and $J_{5'b-5'a} = 12$); 3.84 (s, 3H, OCH_3); 3.92–3.94 (m, 1H, H4′); 4.32 (t, 1H, H3′, J = 5.57); 4.68 (dd, 1H, H2′, $J_{2'-1'} = 4.1$ and $J_{2'-3'} = 5.57$); 5.74 (d, 1H, H1′, $J_{1'-2'} = 4.1$); 7.01 (s, 1H, H5). ^{13}C NMR (CD_3OD; 100MHz) δ: 44.2 (C-5′); 54.3 (OCH_3); 62.6 (C-2′); 63.4 (C-3′); 77.2 (C-4′); 80.2 (C-1′); 110.8 (C-5); 132.3 (C-6); 156.4 (C-4);158.1 (C=O ester); 160.8 (C-2). MS {CI, NH_4^+, M+18 = 337}, (EI), M/z (%): 246 (15); 189 (15); 188 (46); 160 (15); 133 (40); 132 (44); 117 (26); 116 (23); 114 (17); 101 (15); 86 (15); 85 (83); 74 (18); 73 (100); 60 (32); 59 (32); 58 (21); 57 (71); 55 (19); 45 (26); 43 (23); 31 (33); 29 (31). (LSIMS with Cs^+, Positif in Micromasse)-Calcd for $C_{11}H_{13}NO_8S$: $[M + H]^+ = 320.0362$. Found: $[M + H]^+ = 320.0370$.

5-Acetyl-3,6-dihydro-3-(α,β-D-ribofuranosyl)-2*H*-1,3-thiazin-2-one (34). A solution of **30** in THF (5 mL) was treated with tetrabutylammonium fluoride trihydrate (0.33 g, 1.05 mmol). The mixture was stirred at room temperature for 2 h and the solvent was evaporated in vacuo. The crude product was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate (1/1). Dowex 50X2-200 (1 g) was washed twice with methanol and was added to the resulting 3-(2′,3′-*O*-isopropylidene-α,β-ribofuranosyl)-6-acetyl-*2H*-1,3-thiazin-2-one (0.22 g, 0.67 mmol) in solution in methanol (10 mL). The mixture was stirred at room temperature for another 15 h, filtered and the resin was washed thoroughly with methanol. The solution was concentrated in vacuo and the crude product was purified by flash chromatography on silica gel, eluting with ethyl acetate/methanol (98/5), to get α, β-anomeric mixture of **34** in 44% overall yield (α/β ratio = 1/3). α and β **anomers**: ^{1}H NMR (CD_3OD; 200 MHz) δ: 2.55, 2.58 2*(s, 3H, 2*CH_3); 3.84–4.27 (m, 8H, H5′a, H5′b and 2*CH_2); 4.68 (m, 1H,

H4′); 4.82 (m, 1H, H4′); 5.13–5.19 (m, 1H, H3′); 5.43 (d, 1H, H2′); 5.65–5.67 (m, 1H, H3′); 5.07 (d, 1H, H2′); 6.28 (d, 1H, H1′, J = 4.6); 6.33 (d, 1H, H1′, J = 4.8); 7.60, 7.62 2*(s, 1H, H6). ^{13}C NMR (CD_3OD; 50 MHz) δ: 21.0 (CH_3); 23.3 (CH_3); 25.4 (C-4); 26.1 (C-4); 63.3, 63.5 (C-5′); 79.0, 79.2 (C-2′); 81.2 (C-3′); 81.3 (C-3′); 83.0 (C-4′); 87.0 (C-1′); 86.6 (C-4′); 87.4 (C-1′); 113.5, 113.4 (C-5); 139.5 (C-6); 167.8, 169.1 (C-2); 194.6 (C=O). (LSIMS with Cs+, Positif in Micromasse)-Calcd for $C_{11}H_{15}NO_6S$: $[M + H]^+ = 290.0698$. Found: $[M + H]^+ = 290.0698$.

3-(2,3-*O*-Isopropylidene-α,β-D-ribofuranosyl)-4-methyl-2*H*-1,3-thiazolin-2-one (35). A solution of **31**α or **31**β (0.5 g, 0.95 mmol) in THF (5 mL) was treated with tetrabutylammonium fluoride trihydrate (0.36 g, 1.1 mmol). The mixture was stirred at room temperature for 2 h. and the solvent was evaporated in vacuo. The crude product was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate (1/1), to get **35**α or **35**β in 70% yieds. α **anomer**: $[\alpha]_D^{20} = +39.4$ (C = 0.62, $CHCl_3$). ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 1.32 and 1.45 (2s, 2*3H, CMe_2); 2.25 (1H, OH); 3.67–3.78 (m, 2H, H5′a, H5′b); 3.86 (s, 1H, 3H, OCH_3); 4.71–4.76 (m, 1H, H4′); 4.82–4.91 (m, 2H, H2′, H3′); 6.20–6.23 (m, 1H, H1′); 7.00 (s, 1H, H5). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 24.7 et 25.6 ($C(\underline{C}H_3)_2$); 52.9 ($O\underline{C}H_3$); 63.1 (C-5′); 80.3 (C-2′); 81.5 (C-3′); 85.8 (C-4′); 87.8 (C-1′); 115.8 ($\underline{C}(CH_3)_2$); 118.7 (C-5); 140.7 (C-6); 163.9 (C4=O); 165.9 (C=O ester); 167.5 (C2=O). β **anomer**: $[\alpha]_D^{20} = -30.5$ (C = 0.76, $CHCl_3$). ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 1.28 and 1.51 (2s, 2*3H, CMe_2); 2.51 (1H, OH); 3.61–3.80 (m, 5H, H5′a, H5′b, OCH_3); 4.16–4.21 (m, 1H, H4′); 4.87 (dd, 1H, H3′, $J_{3'-4'} = 3.52$, $J_{3'-2'} = 6.4$); 5.05 (dd, 1H, H2′, $J_{2'-3'} = 6.4$, $J_{2'-1'} = 3.36$); 5.86 (d, 1H, H1′, $J_{1'-2'} = 3.36$); 6.98 (s, 1H, H5). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 25.5 and 27.4 ($C(\underline{C}H_3)_2$); 53.1 (CH_3O); 63 (C-5′); 80.8 (C-2′); 82 (C-3′); 86.7 (C-4′); 88.1 (C-1′); 114.6 ($\underline{C}(CH_3)_2$); 120.1 (C-5); 139.7 (C-6); 164.2 (C4=O); 165.6 (C=O ester); 168.7 (C2=O). MS {CI^+, NH_4^+, M+18 = 377}; M/z (%): 344 (65); 116 (15); 86 (23); 85 (52); 71 (17); 69 (24); 68 (32); 59 (77); 57 (39); 43 (100); 41 (29); 31 (34); 29 (27). (LSIMS with Cs^+, Positif in Micromasse)-Calcd for $C_{14}H_{17}NO_6S$: $[M + H]^+ = 359.0753$. Found: $[M + H]^+ = 360.0752$.

4-Methyl-3-(α,β-ribofuranosyl)-2*H*-1,3-thiazolin-2-one (36). Dowex 50X2-200 (0.31g, 0.86 mmol), previously washed twice with methanol, was added to the α or β anomer of **(35)** (88 mg, 0.245 mmol) in solution in methanol (5 mL). The mixture was stirred at room temperature for 15 h, filtered and the resin was washed twice with methanol. The solution was evaporated in vacuo and the crude product was purified by preparative TLC eluting with ethyl acetate to get the ribosyls **36**α or **36**β in 72% yields. δ **anomer**: $[\alpha]_D^{20} = +25,5$ (C = 1, MeOH). ^{1}H NMR ($CDCl_3$; 200 MHz) δ: 2.24 (s, 3H, CH_3); 3.60–3.86 (m, 2H, H5′a, H5′b); 4.39–4.42 (m, 1H, H4′); 4.70–4.81 (m, 2H, H2′, H3′); 6.20 (d, 1H, H1′, J = 3.6); 6.25 (s, 1H, H4). ^{13}C

NMR ($CDCl_3$; 50 MHz) δ: 17.7 (CH_3); 62.4 (C-5′); 79.3 (C-2′); 80.2 (C-3′); 83.6 (C-4′); 100.8 (C-1′); 105.5 (C-4); 146.0 (C-5); 173.2 (C-2). β **anomer**: $[\alpha]_D^{20} = -12{,}3$ (C = 1, MeOH). ^1H NMR ($CDCl_3$; 200 MHz) δ: 2.10 (d, 3H, CH_3, $J_{CH_3\text{-}CH} = 1.1$); 3.58–3.76 (m, 2H, H5′, H5′b); 4.20–4.24 (m, 1H, H4′); 4.90 (dd, 1H, H3′, $J_{3'-4'} = 2.96$, $J_{3'-2'} = 6.1$); 5.20 (dd, 1H, H2′, $J_{2'-1'} = 2.29$, $J_{3'-2'} = 6.1$); 5.40 (d, 1H, H1′, $J_{2'-1'} = 2.29$); 5.70 (q, 1H, H4, $J_{CH\text{-}CH_3} = 1.1$). ^{13}C NMR ($CDCl_3$; 50 MHz) δ: 15.8 (CH_3); 63.0 (C-5′); 81.2 (C-2′); 82.4 (C-3′); 86.5 (C-4′); 91.6 (C-1′); 98.0 (C-4); 132.0 (C-5); 173.9 (C=O). (LSIMS with Cs^+, Positif in Micromasse) -Calcd for $C_9H_{13}NO_5S$: $[M+H]^+ = 247.0514$. Found: $[M+H]^+ = 247.0536$.

REFERENCES

1. a) Perigaud, C.; Gosselin, G.; Imbach, J.-L. Nucleoside Analogues a Chemotherapeutic Agents: A Review. Nucleosides Nucleotides **1992**, *11*, 903. b) Huryn, D.M.; Okabe, M. AIDS_Driven Nucleoside Chemistry. Chem. Rev. **1992**, *92*, 1745.
2. a) Seela, F.; Becher, G.; Rosemeyer, H.; Reuter, H.; Kastner, G.; Mikhailopulo, I.A. The *High-Anti* Conformation of 7-Halogenated 8-Aza-7-deaza-2′-deoxyguanosines: A Study of the Influence of Modified Bases on the Sugar Structure of Nucleosides. Helv. Chim. Acta **1999**, *82*, 105. b) Ramzaeva, N.; Mittelbach, C.; Seela, F. 7-Halogenated 7-Deaza-2′-deoxyinosines. Helv. Chim. Acta **1999**, *82*, 12 and references therein. c) Wigerinck, P.; Van Aerschot, A.; Janssen, G.; Claes, P.; Balzarini, J.; De Clercq, E.; Herdewijn, P. Synthesis and Antiviral Activity of 3′-Herocyclic Substituted 3′-Deoxythymidines. J. Med. Chem. **1990**, *33*, 868. d) Nair, V.; Nuesca, Z.M. Isodideoxynucleosides: A Conceptually New Class of Nucleoside Antiviral Agents. J. Am. Chem. Soc. **1992**, *114*, 7951. e) Sujino, K.; Sugimura, H. Stereocontrolled Synthesis of 3′-Isomeric β-Nucleoside by Intramolecular Glycosylation. J. Chem. Soc., Chem. Commun. **1994**, *11*, 2541 and references therein. f) Kakefuda, A.; Shuto, S.; Nagahata, T.; Seki, J.-I.; Sasaki, T.; Matsuda, A. Synthesis and Biological Evaluations of Ring-Expanded Oxetanocin Analogues: Purine and Pyrimidine Analogues of 1,4-Anhydro-2-deoxy-D-arabitol and 1,4-Anhydro-2-deoxy-3-hydroxymethyl-D-arabitol. Tetrahedron **1994**, *50*, 10167. g) Costa, A.M.; Faja, M.; Farràs, J.; Vilarrasa, J. Uracil- and Thymine-Substituted Thymidine and Uridine Derivatives. Tetrahedron Lett. **1998**, *39*, 1835 and references therein. h) Kasnar, B.; Skaric, V.; Klaic, B.; Zinic, M. A Novel Synthesis of ''Double Headed'' Nucleosides via ''Reversed'' Nucleosides. Tetrahedron Lett. **1993**, *34*, 4997 and references therein. i) Mikhailov, S.; De Clercq, E.; Herdewijn, P. Ribosylation of Pyrimidine 2′-Deoxynucleosides. Nucleosides Nucleotides **1996**, *15*, 1323. j) Derry, W.B.; Pamidi, C.C.; Gupta, R.S. Synthesis and Biological Activity of Novel Thymidine Derivatives of Podophyllotoxin and 4′-Demethylepipodophyllotoxin. Anticancer Drug. Design **1993**, *8*, 203.
3. a) Kovács, L.; Herczegh, P.; Batta, G.; Farkas, I. Thiazole *C*-Nucleosides. III. Synthesis of Pyranose Analogues of Tiazofurin. Tetrahedron **1991**, *47*, 5539.

b) Jung, M.E.; Trifunovich, I.D. Efficient Synthesis of 2′,3′-Dideoxynucleosides and 2′,3′-Dideoxy *C*-Nucleosides from D-Glucosamine. Tetrahedron Lett. **1992**, *33*, 2921.

4. Prestat, G.; Ane, A.; Dubreuil, D.; Pradère, J.P.; Lebreton, J.; Evers, M.; Henin, Y. Synthesis of 3′-O^2-(Azaheterocycle)-Thymidines. Nucleosides Nucleotides **2000**, *19*, 735.
5. a) Boger, D.L.; Weinreb, S.M. *Hetero Diels-Alder Methodology in Organic Synthesis*; Academic Press: 1987; San Diego and references therein. b) Tea, C.G.; Pradère, J.P.; Quiniou, H.; Toupet, L. The Preparation and Rearrangements of 5-Acyl-2-phenyl-4-substituted 6*H*-1,3-Thiazines. *X*-Ray Molecular Structure of 3-Acetyl-2-ethoxycarbonyl-4-(3-oxobutylthio)-5-phenylpyrrole. J. Chem. Soc., Perkin Trans. **1985**, *1*, 1875. c) Pradère, J.P.; Roze, J.C.; Quiniou, H.; Danion-Bougot, R.; Danion, D.; Toupet, L. Des 6*H*-thiazines-1,3 aux CJphPmes par Cyclocondensation. Can. J. Chem. **1986**, *64*, 597. d) Chehna, M.; Pradère, J.P.; Quiniou, H.; Le Botlan, D.; Toupet, L. Substituted 1-Thia-3-aza-1,3-butadiene: Diels-Alder Reaction with Methylacrylate. Determination of Activation Parameters. Phosphorus, Sulfur Silicon Relat. Elem. **1989**, *42*, 15. e) Toure, S.A.; Voglozin, A.; Degny, E.; Danion-Bougot, R.; Danion, D.; Pradère, J.P.; Toupet, L.; N'Guessan, Y.T. Addition de l'ylure de trimèthylsulfoxonium et du mèthylenetriphnylphoshorane aux N^2-thioacylamidines. Bull. Soc. Chim. Fr. **1991**, *128*, 574. f) Tea, C.G.; Chehna, M.; Pradère, J.P.; Duguay, G.; Toupet, L. Thia-1 Aza-3 Butadienes Substitutes: Action du Cetene et Derives. Phosphorus Sulfur Relat. Elem. **1986**, *27*, 327.
6. Analytical data for compound **4** are consistent with thus of the literature: Aubert, P.; Jeffreys, R.A. Knott; E.B. Thiazolid-2: 5-Dione. J. Chem. Soc. **1951**, *2195*.
7. Rosemeyer, H.; Seela, F. Stereoselective Synthesis of Pyrrolo[2,3-*d*]pyrimidine α- and β-D-Ribonucleosides from Anomerically Pure D-Ribofuranosyl Chlorides: Solid-Liquid Phase-Transfer Glycosylation and ^{15}N-NMR Spectra. *Helv. Chim. Acta.* **1988**, *71*, 1573.
8. Jungmann, O.; Pfleiderer, W. A New Efficient Method in Nucleoside Synthesis. Tetrahedron Lett. **1996**, *37*, 8355 and references therein.
9. a) Jung, M.E.; Castro, C. New Approach to the Synthesis of β-2′-Deoxyribonucleosides: Intramolecular Vorbrüggen Coupling. J. Org. Chem. **1993**, *58*, 807. b) Sujino, K.; Sugimura, H. Stereocontrolled Synthesis of β-D-2′-Deoxyribonucleosides by Intramolecular Glycosylation. Chem. Lett. **1993**, 1187. c) Lipshutz, B.H.; Hayakawa, H.; Kato, K.; Lowe, R.F.; Stevens, K.L. A Novel Route to Pyrimidine Nucleosides via Intramolecular Couplings of Bases with 2′-Deoxyribosides: Quick and Sterospecific . . . but with a 'Twist'. Synthesis **1994**, 1476. d) Sujino, K.; Sugimura, H. Sterocontrolled Synthesis of Pyrimidine 2′,3′-Dideoxy-β-nucleosides by Intramolecular Glycosylation Tetrahedron Lett. **1994**, *35*, 1883. e) Lipshutz, B.H.; Stevens, K.L.; Lowe, R.F. A Novel Route to the *anti*-HIV Nucleoside d4T. Tetrahedron Lett. **1995**, *36*, 2711. f) Xia, X.; Wang, J.; Hager, M. W.; Sisti, N. and Liotta, D.C. Stereocontrolled Synthesis of β-2′-Deoxypyrimidine Nucleosides via Intramolecular Glycosylations. Tetrahedron Lett. **1997**, *38*, 1111. g) Lluís, J.; Matheu, M^{a}. I.; Castillón, S. Stereoselective Synthesis of 2′,3′-Dideoxy-nucleosides via Intramolecular

Glycosylation of Phenyl 1-Seleno-glycosides. Synthesis of 2′,3′-Dideoxythymidine. Tetrahedron Lett. **1998**, *39*, 1807. h) Sugimura H.; Katoh, Y. Synthesis of 2′,5′-Dideoxy-5′-substituted Pyrimidine Nucleosides via Intramolecular Glycosylation. Chem. Lett. **1999**, 361.

10. An nOe of 3% was observed between H1′ and H4′ for **26**. No enhancement of either H1′ and H4′ was observed upon irradiation of H4′.
11. Perrin, D.D.; Armarego, W.L.F. *Purification of Laboratory Chemicals*; Pergamon Press: Oxford.

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