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Stereocontrolled Radical Reactions in Carbohydrate and Nucleoside Chemistry.

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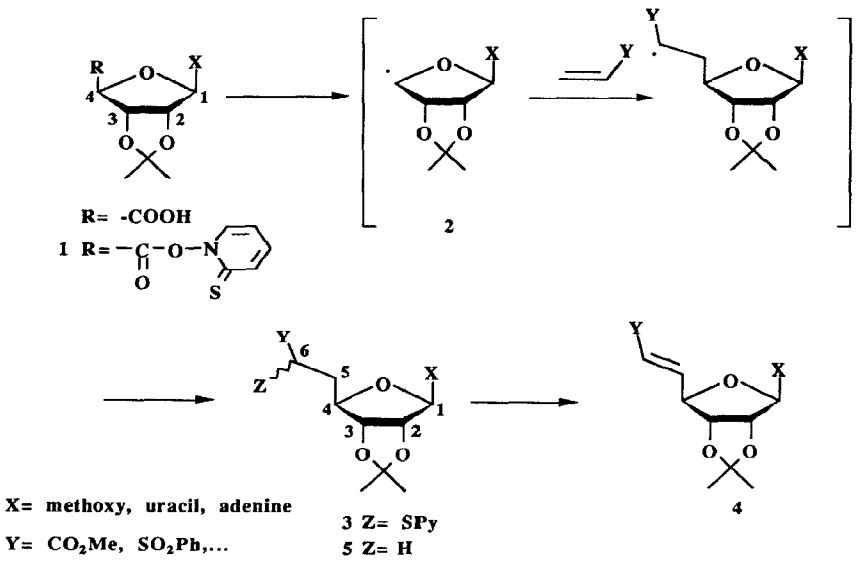
Abstract: The radicals, generated by photolysis of 2,3-dimethyl ketals of N-hydroxy-2-thiopyridone uronic esters, reacted stereoselectively with electron deficient olefins leading to highly functionalised chain-elongated pentafuranosides, hexapyranosides and pentafuranosyl-nucleosides through the 4,5 and 4' radicals, respectively.

It occurred to us that Carbon-Carbon bond formation using free radical reactions might be the most suitable way to synthesize branched-chain sugars and nucleosides[1] with stereochemical control.[2] In this respect, the Barton[3] decarboxylation reaction using thiohydroxamic esters, seemed the method of choice. The thiohydroxamic esters **1** readily obtained from *N*-hydroxy-2-thiopyridone undergo, either on photolysis or heating, a decarboxylation to give a radical **2** which affords in the presence of a suitable trap the addition product **3**. This latter can be considered to have a doubly functionalized carbon. It gives rise to either olefin **4** by oxidation and elimination or might be readily transformed into the desulphurised product **5** using Raney Nickel or tributyltin hydride (Scheme 1).

This reaction scheme can be used for the synthesis of a large variety of carbohydrates and nucleosides, accessible until now only with difficulty. We hoped that the presence of a bulky group such as an isopropylidene acetal adjacent to the radical might control the stereochemical outcome of the newly formed carbon-carbon bond. The importance of steric hindrance in controlling the stereoselectivity of radical reactions has already been observed.[4]

1,2:3,5-Di-*O*-isopropylidene-α-*D*-glucofuranuronic acid **6**, readily obtained by saponification of the corresponding methyl ester,[5] was transformed to its thiohydroxamic ester using the mixed anhydride method[6] (Scheme 2). Irradiation with a tungsten light in the presence of an excess of methyl acrylate gave 57% yield of the expected addition product **7** as a mixture of diastereoisomers at position 7 and a small amount of di-addition product **8** (10%). Oxidation of **7** to the sulfoxide followed by elimination afforded the unsaturated ester **9** as a single product (70%). To prove the retention of configuration at carbon 5, the olefin **9** was oxidized with ruthenium tetroxide to yield the starting uronic acid **6**, identical in all respects with authentic 1,2:3,5-di-*O*-isopropylidene-glucofuranuronic acid. A similar series of reactions was carried out using phenyl vinyl sulphone as a radical trap giving the adduct **10** in 67% yield. The phenyl vinyl sulphone was not subject to polymerization and no di-addition product was observed. After oxidation-elimination, the crystalline unsaturated sulphone **11** was isolated (80%).

In both cases, we were able to control the absolute configuration at carbon 5 but at position 7 as expected we obtained the two epimers. The olefin addition takes place from the opposite side of the acetal group leading to the retention product.



Scheme 1

Likewise, the known 1,2:3,4-di-O-isopropylidene-D-galacturonic acid[7] **12** was transformed in the presence of the appropriate olefin into the addition products **14** (54%) and **16** (65%) from the less hindered side.

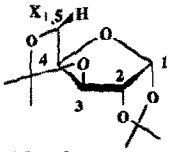
The NMR data of the olefin derivatives **15** (82%) and **17** clearly indicated inversion of configuration at C-5 and also inversion of the chair conformation (chair $^4C_1$ -> chair $^1C_4$; $J_{4,5}$= 10 Hz).

To prove the conformation of the radical and the axial addition of the olefin, the crystalline thiohydroxamic ester derived from *D*-galacturonic acid **13** was photolysed at -25° in tetrahydrofuran. Analysis of the E.P.R. spectrum of the radical suggests that the conformation of the radical is the same as the starting ester (triplet, g= 2.0034 G; aHα= 1.9 mT, aHβ= 0.256 mT). The flip-over of the chair-conformation occurs after the addition of the olefin.

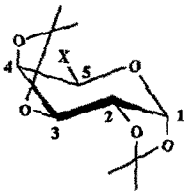
We studied the stereoselectivity of the radical reaction in the absence of an adjacent ketal function. Thus, the thiohydroxamic ester of tetra-acetylglucopyranuronic acid **19** -readily prepared by hydrolysis of 1,2:3,4-tetra-*O*-acetyl-α-*D*-glucuronamide[8] with nitrogen tetroxide- photolysed in the presence of methyl acrylate afforded a mixture of two products **20** and **21** in 70% yield with retention and inversion of configuration at carbon 5 in a 1/1 ratio. The configuration at carbon 5 was established by the NMR data of the corresponding unsaturated esters **22** ($J_{2,3}$= $J_{3,4}$= $J_{4,5}$= 10 Hz) and **23** ($J_{2,3}$= $J_{3,4}$= 5.5 Hz; $J_{4,5}$= 3.5 Hz). It is noteworthy that in the case of phenyl vinyl sulphone as a radical trap only the inversion product **24** (65%) was isolated and characterized as olefin **25** (75%).

In the pentafuranoside series, we also observed the directive effect of the ketal group in controlling the new stereogenic centers. For instance, the thiohydroxamic ester of β-*D*-ribofuranuronic acid **26**[9] gave, with 6 eq of phenyl vinyl sulphone, a mixture of stereoisomers **27** (95%). This latter, on oxidation and elimination, afforded a single crystalline product **28** (60%) with retention of configuration at carbon 4 ($J_{3,4}$= 0 Hz). In contrast the *D*-lyxofuranuronic acid **29**, readily prepared from methyl 2,3-*O*-isopropylidene-α-*D*-mannofuranoside,[10] on addition of the radical to phenyl vinyl sulphone yielded the adduct **30** (95%) in which

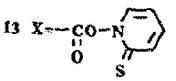
the side chain was inverted. The two products **28** and **31** (60%) are enantiomers as clearly shown by their identical NMR spectral data and the identical value of their specific rotations, with opposite sign.



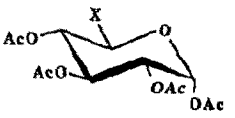
6 X= -COOH
7 X= $-CH_2CH(SPy)CO_2Me$
8 X= $-CH_2CH(CO_2Me)\ CH_2CH(SPy)CO_2Me$
9 X= $-CH{=}CH\text{-}CO_2Me$
10 X= $-CH_2CH(SPy)SO_2Ph$
11 X= $-CH{=}CH\text{-}SO_2Ph$



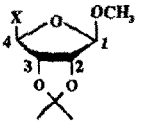
12 X= -COOH



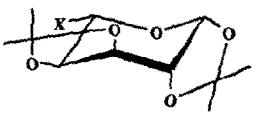
13



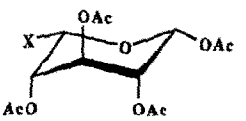
18 X= $-CONH_2$
19 X= -COOH
20 X= $-CH_2CH(SPy)CO_2Me$
22 X= $-CH{=}CH\text{-}CO_2Me$



26 X= -COOH
27 X= $-CH_2CH(SPy)SO_2Ph$
28 X= $-CH{=}CH\text{-}SO_2Ph$

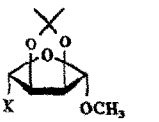


14 X= $-CH_2CH(SPy)CO_2Me$
15 X= $-CH{=}CH\text{-}CO_2Me$
16 X= $-CH_2CH(SPy)SO_2Ph$
17 X= $-CH{=}CH\text{-}SO_2Ph$



21 X= $-CH_2CH(SPy)CO_2Me$
23 X= $-CH{=}CH\text{-}CO_2Me$
24 X= $-CH_2CH(SPy)SO_2Ph$
25 X= $-CH{=}CH\text{-}SO_2Ph$

29



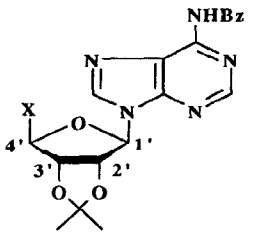
30 X= $-CH_2CH(SPy)SO_2Ph$
31 X= $-CH{=}CH\text{-}SO_2Ph$

Sheme 2

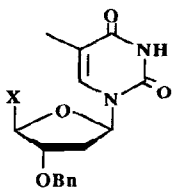
In the nucleoside field, from adenosine[11] and uridine[12] only the retention adducts **32** and **35** were isolated (Scheme 3). In the case of adenosine **32**, we obtained the addition product **33** (60%) which was transformed in the usual way into unsaturated sulphone **34** (60%). Ozonolysis of **34** followed by oxidation of the aldehyde intermediate with mCPBA afforded a carboxylic acid identical with the starting **32**. Likewise, in the presence of methyl acrylate and phenyl vinyl sulphone we obtained the adducts **36** (82%) and **38** (95%) derived from uridine, respectively. Oxidation-elimination of the thiopyridyl group of **36** and **38** yielded the known[13] unsaturated ester **37** (72%) and the sulphone **39** (95%). As before the carbon-carbon bond formation can occur stereoselectively in an anti-addition fashion, leading to the retention products.

In the case of 2'-deoxynucleosides, we expected good stereoselectivity if the position 3' was protected with a bulky group. The 3'-*O*-benzyl-*tert*-butyl ester **40** derived from thymidine was prepared from 3'-O-benzyl-thymidine[14] by the Corey procedure[15]. This ester **40** was hydrolysed with trifluoroacetic acid to yield the crystalline acid **41** (95%). This latter gave in the presence of phenyl vinyl sulphone the diastereoisomers **42** and **44**, isolated in a ratio 6/1 by chromatography. Transformation into the unsaturated sulphones **43** (81%) and **45** (75%) was effected by the well established oxidation-elimination procedure. In order to improve the stereoselectivity, we prepared the acid[16] **46**. Decarboxylation of **46** in the presence of phenyl vinyl sulphone gave a mixture of diastereoisomers **47** and **48** at position 4' with a high stereoselectivity. After oxidation and elimination, we isolated the retention product **49** in 70% yield and the inversion compound **50** in 4% yield.

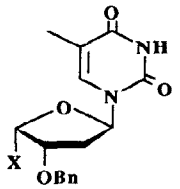
These results show the dominant effect of steric bulk in controlling the chirality of carbon-carbon bond formation using free radical reactions. Anomeric effects may also be involved.[17] We took advantage of this high stereoselectivity to synthesize branched-chain natural products such as sinefungin (S), its (R) epimer at C6'[11], analogues of sinefungin in which the adenosine was replaced by uridine[12b] or thymidine.[18] Lastly the synthesis of the isostere AZT-5' monophosphate[16] was also reported from our laboratory.



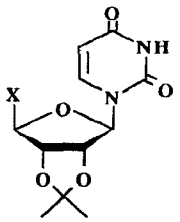
32 X= -COOH
33 X= -$CH_2CH(SPy)SO_2Ph$
34 X= -CH^{t}=CH-SO_2Ph



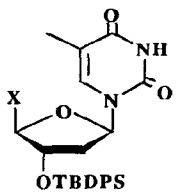
40 X= -$COOC(CH_3)_3$
41 X= -COOH
42 X= -$CH_2CH(SPy)SO_2Ph$
43 X= -CH^{t}=CH-SO_2Ph



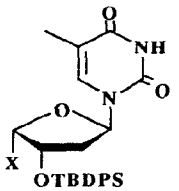
44 X= -$CH_2CH(SPy)SO_2Ph$
45 X= -CH^{t}=CH-SO_2Ph



35 X= -COOH
36 X= -$CH_2CH(SPy)CO_2Me$
37 X= -CH^{t}=CH-CO_2Me
38 X= -$CH_2CH(SPy)SO_2Ph$
39 X= -CH^{t}=CH-SO_2Ph



46 X= -COOH
47 X= -$CH_2CH(SPy)SO_2Ph$
49 X= -CH^{t}=CH-SO_2Ph



48 X= -$CH_2CH(SPy)SO_2Ph$
50 X= -CH^{t}=CH-SO_2Ph

Scheme 3

Experimental

General

Column chromatography was carried out on silica gel 60 (0.040 - 0.063 μm). TLC analysis were performed on thin layer analytical plates 60F254 (Merck). ^1H and ^{13}C NMR spectra were recorded on Bruker WP 200 SY (200 MHz) or at WP 400 (400 MHz). Chemical shifts (δ) are expressed in ppm from Me_4Si as internal standard. Coupling constants *J* are in Hz. Most spectra were taken in $CDCl_3$. In other cases the solvent is specified. E. P. R. spectra were recorded on Bruker ER-420. Melting points were taken on a Reicher apparatus and are uncorrected. Infrared spectra were recorded on a Pelkin-Elmer 297 instrument. Routine mass spectra were recorded on an AEI MS50, AEI MS9 and Kratos MS80 (for FAB spectra). Elemental analyses were carried out in the Institut de Chimie des Sustances Naturelles.

1,2:3,5-di-O-isopropylidene-α-D-glucofuranuronic acid **6**

To a solution of sodium hydroxide 0.33 g (8.5 mmol) in water (20ml) methyl 1,2:3,5-di-*O*-isopropylidene-α-*D*-glucofuranuronate (1.584g, 5.5 mmol) was added. The reaction mixture was stirred at room temperature for 3h and extracted with ether. The aqueous phase was then acidified with citric acid (1.15 g, 2 eq) and extracted with ether (2x100 ml). The organic layer was dried (Na_2SO_4), filtered and evaporated under reduced pressure to yield acid **6** as an oil (1.357 g, 90%). Anal. Calc. for $C_{12}H_{18}O_7.1/2H_2O$, C(50.88); H(6.71). Found: C(50.83); H(6.53). $[\alpha]_D^{20}$= +19.6 (c=1.1; $CHCl_3$). MS (E.I., m/z): 274 $(M)^{+\cdot}$. IR ν_{max} ($CHCl_3$) : 1736 cm^{-1}. ^1H RMN (400 MHz, $CDCl_3$): δ ppm: 6.04 (d, 1H, H_1, $J_{1,2}$= 4 Hz); 4.63 (dd, 1H, H_4, $J_{4,5}$= 5.5 Hz, $J_{4,3}$= 3 Hz); 4.46 (d, 1H, H_2, $J_{2,1}$= 4 Hz); 4.28 (d, 1H, H_3, $J_{3,4}$= 3 Hz); 4.27 (d, 1H, H_5, $J_{5,4}$= 5.5 Hz); 1.5, 1.43, 1.33 (3s, 12H, 2 CMe_2).

1,2:3,4-Tetra-O-acetyl-α-D-glucuronamide **18**

To a solution of glucuronamide (5 g, 25.9 mmol.) in pyridine (18 ml) was added at 0°C, acetic anhydride (18 ml). The mixture was stirred at 30°C for 6h and at room temperature overnight. The mixture was then poured into cooled water and extracted with chloroform. The organic layer was dried (Na_2SO_4), filtered and evaporated under reduced pressure. The residue was co-evaporated with toluene to remove pyridine and was crystallized from dichloromethane-hexane to afford **18** (8.41 g, 90%); mp 147-149°C (CH_2Cl_2-hexane); lit.[8] 154-156°C (CH_2Cl_2-hexane). IR: ν_{max} (nujol): 3477, 1755, 1750, 1645 cm^{-1}. MS (E.I., m/z): 361 $(M)^{+\cdot}$. ^1H RMN (200MHz, $CDCl_3$): δ ppm: 6.43 (d, 1H, H_1, $J_{1,2}$= 4 Hz); 5.58 (t, 1H, H_3, $J_{3,4}$= 10 Hz, $J_{3,2}$= 10 Hz); 5.28 (t, 1H, H_4, $J_{4,3}$= $J_{4,5}$= 10 Hz); 5.16 (dd, 1H, H_2, $J_{2,1}$= 4 Hz, $J_{2,3}$= 10 Hz); 4.33 (d, 1H, H_5, $J_{5,4}$= 10 Hz); 2.20, 2.08, 2.05 (3s, 12H, $OCO\underline{CH_3}$).

1,2:3,4-Tetra-O-acetyl-α-D-glucopyranuronic acid **19**

To a mixture of amide **18** (7.22 g, 20 mmol.) and potassium acetate (1.96 g, 40 mmol.) in dry dichloromethane (30 ml) was added, dropwise at -20°C during 1h, a solution of nitrogen dioxide (10 ml) in 20% dichloromethane. The mixture was stirred at 0°C for 2h and filtered. The solvent was evaporated to dryness and the residue was dissolved in ether. The organic layer was washed with 40 ml of a 5% sodium hydrogen carbonate solution. The aqueous phase was washed with ether and acidified at 0°C with HCl (2N). The precipitate thus obtained was filtered off, washed with water and dried to give acid **19** (5 g). The filtrate was extracted with ether and the organic layer was dried (Na_2SO_4), filtered and evaporated under reduced pressure to yield acid **19** (0.5 g). The solid was crystallized from dichloromethane-hexane (5.5 g, 75%). Anal.

Calc. for $C_{14}H_{18}O_{11}$. H_2O, C(44.21); H(5.26). Found: C(44.51); H(5.30). $[\alpha]_D^{20}$= + 92 (c=1; $CHCl_3$); mp 74-76°C (CH_2Cl_2-hexane). IR: ν_{max} (nujol): 3497, 3367, 1755, 1700 cm^{-1}. MS (E.I., m/z): 362 $(M)^{+\cdot}$, 345 $(M-17)^{+\cdot}$. ^1H RMN (200MHz, $CDCl_3$): δ ppm: 6.48 (d, 1H, H_1, $J_{1,2}$= 4 Hz); 5.57 (t, 1H, H_3, $J_{3,4}$= 10 Hz, $J_{3,2}$= 10 Hz); 5.31 (t, 1H, H_4, $J_{4,3}$= 10 Hz, $J_{4,5}$= 10 Hz); 5.16 (dd, 1H, H_2, $J_{2,1}$= 4 Hz, $J_{2,3}$= 10 Hz); 4.46 (d, 1H, H_5, $J_{5,4}$= 10 Hz); 2.19, 2,06, 2,03 (3s, 12H, $OCO\underline{CH_3}$).

Methyl-2,3-O-isopropylidene-α-D-lyxofuranosiduronic acid 29

A mixture of *D*-mannose (5 g, 27.77 mmol), 2,2-dimethoxypropane (17 ml), acetone (16.5 ml), methanol (16.5 ml) and concentrated HCl (0,5 ml) was refluxed for 2 h. The cooled mixture was diluted with water (50 ml) and concentrated under reduced pressure at below 30°C. Methanol (50 ml) and concentrated HCl (1.25 ml) was then added. The reaction mixture was stirred at room temperature for 3h, neutralized with a saturated sodium hydrogen carbonate solution and evaporated to dryness. The residue was taken in hot chloroform and the solution was filtered through a celite pad. The solvent was evaporated to give methyl-2,3-*O*-isopropylidene-mannofuranoside as a colorless oil (5.43 g, 83%).

Sodium periodate (5.46 g, 25.52 mmol.) dissolved in a minimum of water was added to a solution of methyl-2,3-*O*-isopropylidene-mannofuranoside (5.43 g) in methanol (150 ml). The mixture was stirred for 2 h at room temperature and the solvent was evaporated under reduced pressure. The residue was taken in acetone and the solution was filtered through a celite pad. The filtrate was evaporated to dryness to give the intermediate aldehyde. To the residue dissolved in water (120 ml) a solution of NaOH (0.23 g) in water (5 ml) and a solution of sodium permanganate (7.332 g, 46.4 mmol.) in water (200 ml) were added at 0°C . The mixture was stirred at room temperature for 16h. The excess of potassium permanganate was removed with a solution of H_2O_2 (33%) and the mixture was filtered through a celite pad. The filtrate was concentrated to 100 ml and washed twice with ethyl acetate (100 ml). The aqueous layer was acidified to pH 3 at 0°C with HCl (1N) and extracted with ether (2x100 ml). The organic layer was washed with a saturated sodium chloride solution, dried (Na_2SO_4), filtered and evaporated under reduced pressure to yield acid **29** as a colorless oil (4 g, 79%). Anal. Calc. for $C_{29}H_{14}O_6$. C(49.54); H(6.42). Found: C(49.38); H(6.41). $[\alpha]_D^{20}$= + 19.9 (c= 2.47; $CHCl_3$). IR: ν_{max} (film): 3500, 3210; 1750 cm^{-1}. MS: (C.I., m/z): 219 $(MH)^+$, 187 $(MH\text{-}MeOH)^+$. ^1H RMN (200 MHz, $CDCl_3$):δ ppm: 9.45 (s, 1H, COOH); 5.15 (s, 1H, H_1); 5.11 (dd, 1H, H_3, $J_{3,2}$= 5 Hz, $J_{3,4}$= 4 Hz); 4.68 (d, 1H, H_4, $J_{4,3}$= 4 Hz); 4.65 (d, 1H, H_2, $J_{2,3}$= 5 Hz), 3.4 (s, 3H, OMe); 1.46, 1.33 (2s, 6H, CMe_2).

General procedure for radical addition to olefins

To the acid (1 mmol) in anhydrous tetrahydrofuran (10 mL) was added *N*-methylmorpholine (0.11 ml, 1 mmol) and isobutyl chloroformate (0.14 ml, 1 mmol). After stirring for 15 min at 0° under argon the sodium salt of *N*-hydroxy-2-thiopyridone (0.178 g, 1.2 mmol) was added. The reaction mixture was stirred under argon at 0° for 1 h with exclusion of light (aluminium foil). The mixture was then transfered dropwise to a solution of olefin (5 or 6 mmol.) and the yellow solution was irradiated with a tungsten lamp (250 watts) at 0° for 30 minutes. The reaction mixture was diluted with ether (In the case of carbohydrates) and with chloroform (for nucleosides) (100 ml) and washed with a saturated sodium hydrogen carbonate solution (50 ml) and with water (50 ml). The organic phase was dried over Na_2SO_4 and, after filtration, was evaporated under reduced pressure. The residue thus obtained was chromatographed on a silica gel column.

General procedure for oxidation-elimination of thiopyridyl group

To the addition product (1 mmol.) in dichloromethane (5 ml) was added at 0°C a solution of *m*-chloroperbenzoic acid (1.2 mmol.) in dichloromethane (2 ml). The reaction mixture was stirred at 0°C for 1h and was diluted with dichloromethane and washed with a saturated sodium hydrogen carbonate solution, with

water and then with a saturated sodium chloride solution. The organic phase was dried over Na_2SO_4 and, after filtration, was evaporated under reduced pressure. The sulfoxide was obtained quantitatively and dissolved in dry toluene. The solution was refluxed for 1h, then evaporated under reduced pressure. The residue thus obtained was chromatographed on a silica gel column.

Methyl 6,7-dideoxy-1,2:3,5-di-O-isopropylidene-7-(2'-thiopyridyl)-α-D-gluco-octofuranuronate **7**

Acid **6** (2 mmol.); methyl acrylate (6 eq.). The adduct **7** was isolated as a colorless oil (0.485 g, 57%) (chromatographed: hexane-ethyl acetate, 9-1). Anal. Calc. for $C_{20}H_{27}NO_7S$. C(56.47); H(6.35); N(3.29). Found: C(56.75); H(6.60); N(3.19). IR: ν_{max} ($CHCl_3$): 1731 cm-1. MS (E.I., m/z): 425 $(M)^{+\cdot}$, and the di-addition product **8** (0.103 g, 10%) (chromatographed: hexane-ethyl acetate, 7-3).MS (E.I., m/z): 511 $(M)^{+\cdot}$.

Methyl 6,7-dideoxy-1,2:3,5-di-O-isopropylidene-α-D-gluco-6-ene-octofuranuronate **9**

0.302 g (0.71 mmol) of addition product **7** was used. The unsaturated ester **9** was isolated as a colorless oil (0.161 g, 72%) (chromatographed: hexane-ethyl acetate, 9-1). Anal. Calc. for $C_{15}H_{22}O_7$. C(57.32); H(7.00). Found: C(57.53); H(7.03). $[\alpha]_D^{20}$= +27 (c= 1.44; $CHCl_3$). IR: ν_{max} ($CHCl_3$): 1716 cm^{-1}. MS (E.I., m/z): 314 $(M)^{+\cdot}$. ^1H RMN (400 MHz, $CDCl_3$): δ ppm: 7.03 (dd, 1H, H_6, $J_{6,7}$= 16 Hz, $J_{6,5}$= 4 Hz); 6.1 (dd, 1H, H_7, $J_{7,6}$= 16 Hz, $J_{5,7}$= 2 Hz); 6.01 (d, 1H, H_1, $J_{1,2}$= 4 Hz); 4.58 (d, 1H, H_2, $J_{1,2}$= 4 Hz); 4.28 (q, 1H, H_4, $J_{4,5}$= 7 Hz, $J_{4,3}$= 4 Hz); 4.23 (d, 1H, H_3, $J_{3,4}$= 4 Hz); 4.18 (qd, 1H, H_5, $J_{5,6}$= 4 Hz, $J_{5,4}$= 7 Hz, $J_{5,7}$= 2 Hz); 3.73 (s, 3H, COOMe); 1.47, 1.38, 1.35, 1.33 (s, 12H, 2 CMe_2).

6,7-Dideoxy-1,2:3,5-di-O-isopropylidene-7-phenylsulphonyl-7-(2'-thiopyridyl)-α-D-gluco-heptofuranose **10**

Acid **6** (0.47, 1.52 mmol.); phenyl vinyl sulphone (5 eq.). The adduct **10** was isolated as a colorless oil (0.516 g, 67%) (chromatographed: hexane-ethyl acetate, 8-2). Anal. Calc. for $C_{24}H_{29}NO_7S_2$. C(56.80); H(5.70); N(2.76); S(12.62). Found: C(56.92); H(5.82); N(2.69); S(12.37). IR: ν_{max} ($CHCl_3$): 3677, 1601, 1581, 911 cm^{-1} . MS: (E.I., m/z): 507 $(M)^{+\cdot}$.

6,7-Dideoxy-1,2:3,5-di-O-isopropylidene-7-phenylsulphonyl-α-D-gluco-6-ene-heptofuranose **11**

0.490 g (0.966 mmol) of addition product **10** was used. The unsaturated ester **11** was isolated as crystals (0.31 g, 81%) (chromatographed: hexane-ethyl acetate, 8-2). Anal. Calc. for $C_{19}H_{24}O_7S$. C(57.57); H(6.06); S(8.08). Found: C(57.80); H(5.84); S(8.14). $[\alpha]_D^{20}$= +42 (c = 0.5; $CHCl_3$); mp 145-146°C (ether-pentane). IR: ν_{max} (nujol): 1315, 1145, 1080, 720, 680 cm^{-1}. SM: (C.I., m/z): 397 $(MH)^+$. ^1H RMN (400 MHz,$CDCl_3$): δ ppm: 7.91, 7.76 (m, 5H, Ph); 7.11 (dd, 1H, H_6, $J_{6,7}$= 15 Hz, $J_{6,5}$= 3 Hz); 6.62 (dd, 1H, H_7, $J_{7,5}$= 2 Hz, $J_{7,6}$= 16 Hz); 6.01 (d, 1H, H_1, $J_{1,2}$= 3,5 Hz); 4.59 (d, 1H, H_2, $J_{2,1}$= 3.5); 4.28 (q, H_4, $J_{4,3}$= $J_{4,5}$= 4 Hz); 4.22 (m, 2H, H_3, H_5); 1.48, 1.35, 1.33, 1.32 (4s, 12H, 2CMe).

N-hydroxy-2'-thiopyridyl ester of 1,2:3,4-di-O-isopropylidene-α-D-galacto-pyranuronic acid **13**

To the acid **12** (0.822, 3 mmol) in anhydrous tetrahydrofuran (15 mL) was added under argon *N*-methylmorpholine (0.33 ml, 3 mmol) and isobutyl chloroformate (0.42 ml, 3 mmol). After stirring for 15 min at 0° under argon the sodium salt of *N*-hydroxy-2-thiopyridone (0.534 g, 3.6 mmol) was added. The reaction mixture was stirred under argon at 0° for 1 h with exclusion of light (aluminium foil). The mixture was filtered rapidly and the solvent was evaporated under reduced pressure without heating and with exclusion of light . The oily residue was precipitated from ether-pentane. The precipitate was filtered off, washed with pentane and dried to afford the thiohydroxamic ester **13** (1.034 g, 90%). MS (C.I., m/z): 384 $(MH)^+$, 340 $(MH\text{-}CO_2)^+$. MS (FAB): 384 $(MH)^+$.^1H RMN (200 MHz,$CDCl_3$): δ ppm: 7.76, 7.30, 6.75 (m, 4H, Spy); 5.73 (d, 1H, H_1, $J_{1,2}$= 2.25 Hz); 5.00 (s, 1H, H_5); 4.78 (s, 2H, H_3, H_4), 4.46 (d, 1H, H_2); 1.6, 1.5, 1.38 (s, 12H, 2 CMe_2).

Methyl 6,7-Dideoxy-1,2:3,4-di-O-isopropylidene-7-(2'-thiopyridyl)-α-L-galacto-octopyranuronate ***14***

Acid **12** (0.411 g, 1.5 mmol.) and methyl acrylate (6 eq.) were used. The adduct **14** was isolated as a colorless oil (0.345 g, 54%) (chromatographed: hexane-ethyl acetate, 9,1). Anal. Calc. for $C_{20}H_{27}NO_7S$. C(56.47); H(6.35); N(3.29); S(7.52). Found: C(56.72); H(6.28); N(3.01); S(7.57). IR: ν_{max} ($CHCl_3$): 1731, 1580 cm ^{1}. MS (C.I., m/z): 426 $(MH)^+$.

Methyl 6,7-Dideoxy-1,2:3,4-di-O-isopropylidene-6-ene-α-L-galacto-octopyranuronate ***15***

0.226 g (0.53 mmol) of addition product **14** was used. The olefin **15** was isolated as crystals (0.136g, 82%) (chromatographed: hexane-ethyl acetate, 9-1). Anal. Calc. for $C_{15}H_{22}O_7$. C(57.32); H(7.00). Found: C(57.25); H(7.11). $[\alpha]_D^{20}$= -93 (c=2.4; $CHCl_3$); mp 68-70°C (pentane). IR: ν_{max} ($CHCl_3$): 1718, 1666 cm^{-1}. MS (C.I., m/z): 315 $(MH)^+$. ^{1}H RMN (200 MHz,$CDCl_3$): 7.11 (dd, 1H, H_6, $J_{6,7}$= 16 Hz, $J_{6.5}$= 3.5 Hz); 6.23 (dd, 1H, $J_{7,6}$= 16 Hz, $J_{7,5}$= 1.5 Hz); 5.36 (d, 1H, H_1, J= 2.5 Hz); 4.61 (d, 1H, H_4, $J_{4,5}$= 10 Hz, $J_{4,3}$= 4.5 Hz); 3.88 (dd, 1H, H_5, $J_{5,6}$= 3.5 Hz, $J_{5,4}$= 10 Hz, $J_{5,7}$= 4.5 Hz); 3.78 (s, 3H, OCH_3); 1.55, 1.51, 1.41, 1.38 (4s, 12H, 2 CMe_2).

6,7-Dideoxy-1,2:3,4-di-O-isopropylidene-7-phenylsulphonyl-7-(2'-thiopyridyl)-α-L-galacto-heptopyranose ***16***

Acid **12** (0.548 g, 2 mmol.) and phenyl vinyl sulphone (5 eq.) were used. The adduct **16** was isolated as a colorless oil (0.660 g, 65%) (chromatographed: hexane-ethyl acetate, 8-2). Anal. Calc. for $C_{24}H_{29}NO_7S_2$. C(56,80); H(5.70); N(2.76); S(12.62). Found: C(56.96); H(5.70); N(2.82); S(12.44). IR: ν_{max} (nujol): 1580, 1420, 1310, 1220, 1145, 1065, 860, 735, 680 cm^{-1}. MS (C.I., m/z): 508 $(MH)^+$.

6,7-Dideoxy-1,2:3,4-di-O-isopropylidene-7-phenylsulphonyl-α-L-galacto-6-ene-heptopyranose ***17***

0.507 g (1 mmol) of addition product **16** was used. The olefin **17** was isolated as white foam (0.297 g, 75%) (chromatographed: hexane-ethyl acetate, 8-2). Anal. Calc. for $C_{19}H_{24}O_7S$. C(57.57); H(6.06); S(8.08). Found: C(57.38); H(5.79); S(8.38). $[\alpha]_D^{20}$= -102 (c= 1.47; $CHCl_3$). IR: ν_{max} ($CHCl_3$): 1380, 1300,1140, 1110, 960, 860 cm^{-1}. MS (C.I., m/z): 397 $(MH)^+$. ^{1}H RMN (200 MHz,$CDCl_3$): δ ppm: 7.91, 7.60 (m, 5H, Ph); 7.15 (dd, 1H, H_6, $J_{6,5}$= 2 Hz, $J_{6,7}$= 15 Hz); 6.83 (dd, 1H, H_7, $J_{7,5}$= 1 Hz); 5.25 (d, 1H, H_1, $J_{1,2}$= 2,25 Hz); 4.55 (d, 1H, H_3, $J_{3,4}$= 4 Hz); 4.25 (d, 1H, H_2, $J_{2,1}$= 2.25 Hz); 3.94 (dd, 1H ,H_4, $J_{4,5}$= 10 Hz, $J_{4,3}$= 4 Hz); 3.90 (dd, 1H, H_5, $J_{5,4}$= 10 Hz, $J_{5,6}$= 2 Hz); 1.49, 1.35 (s, 12H, 2 CMe_2).

Methyl 6,7-dideoxy-1,2:3,4-tetra-O-acetyl-7-(2'-thiopyridyl)-α-D-gluco-octopyranuronate ***20*** *and Methyl 6,7-Dideoxy-1,2:3,4-tetra-O-acetyl-7-(2'-thiopyridyl)-α-L-ido-octopyranuronate* ***21***

Acid **19** (0.362, 1 mmol.); methyl acrylate (6eq.). The adduct **20** was isolated as a colorless oil (0.180 g, 35%) (chromatographed: hexane-ethyl acetate, 7-3). Anal. Calc. for $C_{22}H_{27}NO_{11}S$. C(51.46); H(5.26); N(2.72); S(6.23). Found: C(51.25); H(5.01); N(2.72); S(6.46). IR: ν_{max} ($CHCl_3$): 1716 cm^{-1}. MS (I.C., m/z): 514 $(MH)^+$. The second adduct was the inverted product **21** (0.18 g, 35%). MS (I.C., m/z): 514 $(MH)^+$.

Methyl 6,7-dideoxy-1,2:3,4-tetra-O-acetyl-7-α-D-gluco-6-ene-octopyranuronate ***22***

0.162 g (0.317 mmol) of addition product **20** was used. The unsaturated ester **22** was isolated as crystals (0.092 g, 72%) (chromatographed: hexane-ethyl acetate, 7-3). Anal. Calc. for $C_{17}H_{22}O_{11}$. C(50.47); H(5.47). Found: C(50.66); H(5.60). $[\alpha]_D^{20}$= +100 (c = 1; $CHCl_3$). mp 190-192°C (chloroform-hexane). IR: ν_{max} ($CHCl_3$): 1735, 1660 cm^{-1}. MS (E.I., m/z): 402 $(M)^+$. ^{1}H RMN (200 MHz,$CDCl_3$): δ ppm: 6.73 (dd, 1H, H_6, $J_{6,7}$= 16 Hz); 6.36 (d, 1H, H_1, $J_{1,2}$= 4Hz); 6.1(d, 1H, H_7, $J_{6,7}$= 16 Hz); 5.5 (t, 1H, H_3, $J_{3,4}$= 10 Hz); 5.08 (dd, 1H, H_2, $J_{1,2}$= 4 Hz, $J_{2,3}$= 10 Hz); 4.93 (t, 1H, H_5, $J_{4,5}$= 10 Hz, $J_{5,6}$= 5 Hz); 3.75 (s, 3H, OMe); 2.18, 2.06, 2.03 (3s, 12H, $OCOCH_3$).

Methyl 6,7-dideoxy-1,2:3,4-tetra-O-acetyl-7-α-L-ido-6-ene-octopyranuronate 23

0.180 g (0.35 mmol) of addition product **21** was used. The unsaturated ester **23** was isolated as crystals (0.099 g, 70%) (chromatographed: hexane-ethyl acetate, 4-6). Anal. Calc. for $C_{17}H_{22}O_{11}$. C(50.47); H(5.47). Found: C(50.67); H(5.63). $[\alpha]_D^{20}$= +12 (c = 0.5; $CHCl_3$). mp 132-134°C (ether-pentane). IR: ν_{max} (nujol): 1750, 1660 cm^{-1}. MS (C.I., m/z): 344 $(MH\text{-}OCOCH_3)^+$; in presence of NH_3, 420 $(MH+NH_3)^+$. ^1H RMN (400 MHz,$CDCl_3$): δ ppm: 6.92 (dd, 1H, H_6, $J_{6,7}$= 15.5 Hz, $J_{6,5}$= 6 Hz); 6.15 (d, 1H, H_7, $J_{7,6}$= 15.5 Hz); 6.13 (d, 1H, H_1, $J_{1,2}$= 2.5 Hz); 5.35 (t, 1H, H_3, $J_{3,4}$= 5.5 Hz, $J_{3,2}$= 5.5 Hz); 5.03 (dd, 1H, H_2, $J_{2,3}$= 5.5 Hz, $J_{2,1}$= 2.5 Hz); 4.97 (dd, 1H, H_4, $J_{4,3}$= 5.5 Hz, $J_{4,5}$= 3,5 Hz); 4.8 (m, 1H, H_5); 3.75 (s, 3H, OMe); 2.13, 2.03 (s, 12H, $OCOCH_3$).

6,7-Dideoxy-1,2:3,4-tetra-O-acetyl-7-phenylsulphonyl-7-(2'-thiopyridyl)-α-L-ido-heptopyranose 24

Acid **19** (0.362, 1 mmol.) and phenyl vinyl sulphone (5 eq.) were used. The adduct **24** was isolated as an oil (0.405 g, 68%) (chromatographed: hexane-ethyl acetate, 4-6). Anal. Calc. for $C_{26}H_{29}NO_{11}S_2$. C(52.43); H(4.87); N(2.35); S(10.75). Found: C(52.36); H(4.92); N(2.50); S(10.69). IR: ν_{max} ($CHCl_3$): 1751, 1581 cm^{-1}.MS (E.I., m/z): 596 $(MH)^+$.

6,7-Dideoxy-1,2:3,4-tetra-O-acetyl-7-phenylsulphonyl-7-α-L-ido-6-ene-heptopyranose 25

0.357 g (0.6mmol) of addition product **24** was used. The olefin **25** was isolated as crystals (0.198g, 68%) (chromatographed: hexane-ethyl acetate, 4-6). Anal. Calc. for $C_{21}H_{24}NO_{11}S$. C(52.06); H(4.95); S(6.61). Found: C(52.08); H(5.06); S(6.70). $[\alpha]_D^{20}$= +9 (c= 0.5, $CHCl_3$). mp 73-75°C (ether-pentane). IR: ν_{max} (nujol): 1210, 1150, 1050, 720, 690 cm^{-1}. MS (E.I., m/z): 484 $(M)^+$.. ^1H RMN (400 MHz,$CDCl_3$): δ ppm: 7.99, 7.61 (m, 5H, Ph); 6.88 (dd, 1H, H_6, $J_{6,7}$=15 Hz, $J_{6,5}$= 5 Hz); 6.73 (d, 1H, H_7, $J_{7,6}$= 15 Hz); 6.1 (d, 1H, H1, $J_{1,2}$= 2 Hz); 5.25 (t, 1H, H_3, $J_{3,2}$= 4 Hz, $J_{3,4}$= 4 Hz); 4.99 (dd, 1H, H_2, $J_{2,3}$= 4 Hz, $J_{2,1}$= 2 Hz); 4.91 (t, 1H, H_4, $J_{4,3}$= 4 Hz, $J_{4,5}$= 4 Hz); 4.84 (m, 1H, H_5, $J_{5,6}$= 4 Hz); 2.15, 2.13, 1.87 (s, 12H, $OCOCH_3$).

Methyl 5,6-dideoxy-2,3-isopropylidene-6-phenylsulphonyl-6-(2'-thiopyridyl)-β-D-ribo-hexofuranoside 27

Acid **26** (0.218, 1 mmol.) and phenyl vinyl sulphone (5 eq.) were used. The adduct **27** was isolated as an oil (0.430 g, 95%) (chromatographed: hexane-ethyl acetate, 7.5-2.5). Anal. Calc. for $C_{21}H_{25}NO_6S_2$. C(55.87); H(5.54); N(3.10); S(14.19). Found: C(56.07); H(5.51); N(3.08); S(13.98). IR: ν_{max} ($CHCl_3$): 1580, 1770, 1140, 960, 860 cm^{-1}. MS (C.I., m/z): 452 $(MH)^+$, 420 $(MH\text{-}MeOH)^+$.

Methyl 5,6-dideoxy-2,3-isopropylidene-6-phenylsulphonyl-β-D-ribo-5-ene-hexofuranoside 28

0.361 g (0.8 mmol) of addition product **27** was used. The unsaturated ester **28** was isolated as crystals (0.17 g, 62%) (chromatographed: hexane-ethyl acetate, 8-2). Anal. Calc. for $C_{16}H_{20}O_6S$. C(56.47); H(5.88); S(9.41). Found: C(56.57); H(5.97); S(9.24). $[\alpha]_D^{20}$= +2.4 (c= 0.5; $CHCl_3$). mp 118-120°C (ether-pentane). IR: ν_{max}(nujol): 1380, 1090, 870, 755, 690 cm^{-1}. MS (C.I., m/z): 341 $(MH)^+$; 309 $(MH\text{-}MeOH)^+$. ^1H RMN (200 MHz, $CDCl_3$): δ ppm: 7.83, 7.53 (m, 5H, Ph); 6.9 (dd, 1H, H_5, $J_{5,6}$= 15 Hz, $J_{5,4}$= 6 Hz); 6.5 (dd, 1H, H_6, $J_{6,5}$= 15 Hz, $J_{6,4}$= 1.5 Hz); 4.98 (s, 1H, H_1); 4.75 (dd, 1H, H_4, $J_{4,5}$= 6 Hz, $J_{4,6}$= 1.5 Hz); 4.66 (d, 1H, H_3, $J_{3,2}$= 6 Hz); 4.57 (d, 1H, H_2, $J_{2,3}$= 6 Hz); 3.25 (s, 3H, OCH_3); 1.48,1.28 (2s, 6H, CMe_2).

Methyl 5,6-Dideoxy-2,3-isopropylidene-6-phenylsulphonyl-6-(2'-thiopyridyl)-α-L-lyxo-hexofuranoside 30

Acid **29** (0.303, 1.38 mmol.) and phenyl vinyl sulphone (5 eq.) were used. The adduct **30** was isolated as a colorless oil (0.592 g, 95%) (chromatographed: hexane-ethyl acetate, 7.5-2.5). Anal. Calc. for $C_{21}H_{25}NO_6S_2$. C(55.87); H(5.54); N(3.10). Found: C(55.87); H(5.63); N(3.26). IR: ν_{max} ($CHCl_3$): 1580, 1370, 1140, 960, 860 cm^{-1}. MS (C.I., m/z): 452 $(MH)^+$, 420 $(MH\text{-}MeOH)^+$.

Methyl 5,6-Dideoxy-2,3-isopropylidene-6-phenylsulphonyl-α-L-lyxo-5-ene-hexofuranoside 31

0.451 g (1 mmol) of addition product **30** was used. The unsaturated ester **31** was isolated as crystals (0.17 g, 50%) (chromatographed: hexane-ethyl acetate, 8-2). Anal. Calc. for $C_{16}H_{20}O_6S$. C(56.47); H(5.88); S(9.41). Found: C(56.33); H(5.63); S(9.71). mp 118-120°C (ether-pentane). $[\alpha]_D^{20}$= -2.4 (c= 0.5; $CHCl_3$). IR: ν_{max} (nujol): 1320, 1090, 870, 755, 690 cm^{-1}. MS (C.I, m/z): 341 $(MH)^+$, 309 $(MH\text{-}MeOH)^+$. ^1H RMN (200 MHz, $CDCl_3$): δ ppm: 7.83, 7.53 (m, 5H, Ph); 6.9 (dd, 1H, H_5, $J_{5,6}$= 15 Hz, $J_{5,4}$= 6 Hz); 6.5 (dd, 1H, H_6, $J_{6,5}$= 15 Hz, $J_{6,4}$= 1.5 Hz); 4.98 (s, 1H, H_1); 4.75 (dd, 1H, H_4, $J_{4,5}$= 6 Hz, $J_{4,6}$= 1.5 Hz); 4.66 (d, 1H, H_3, $J_{3,2}$= 6 Hz); 4.57 (d, 1H, H_2, $J_{2,3}$= 6 Hz); 3.25 (s, 3H, OCH_3); 1.48, 1.28 (2s, 6H, CMe_2).

(5',6'-dideoxy-2',3'-O-isopropylidene-6'-phenylsulphonyl-6'-(2'-thiopyridyl)-β-D-ribo-5'-ene-hexofuranosyl)-9-N^6-Benzoyl-adenine 33

Acid **32** (0.425, 1 mmol.) and phenyl vinyl sulphone (5 eq.) were used. The adduct **33** was isolated as crystals (0.395 g, 60%) (chromatographed: hexane-ethyl acetate, 2, 8). Anal. Calc. for $C_{32}H_{30}N_6O_6S_2$. C(58.35); H(4.55); N(12.76); S(9.72). Found: C(58.30); H(4.82); N(12.64); S(9.66); mp: 105-108°C (CH_2Cl_2-pentane).

(5',6'-Dideoxy-2',3'-O-isopropylidene-6'-phenylsulphonyl-β-D-ribo-5'-ene-hexofuranosyl)-9-N^6-Benzoyl-adenine 34

0.329 g (0.5 mmol) of addition product **33** was used. The unsaturated ester **34** was isolated as crystals (0.165 g, 60%) (chromatographed: hexane-ethyl acetate, 2.5-7.5). Anal. Calc. for $C_{27}H_{25}N_5O_6S$. C(59.29); H(4.57); N(12.79); S(5.85). Found: C(59.07); H(4.81); N(13.00); S(5.80); mp 115-118°C (CH_2Cl_2). $[\alpha]_D^{20}$= + 94 (c= 0.5; $CHCl_3$). IR: ν_{max} (nujol): 1690, 1610, 1580, 1510, 1150, 1085 cm^{-1}. MS (F.A.B., m/z): 548 $(MH)^+$. ^1H RMN (200 MHz, $CDCl_3$): δ ppm: 9.28 (br s, 1H, NHCOPh); 8.6 (s, 1H, H_2); 8.08 (s, 1H, H_8); 7.75, 7.56 (m, 10H, Ph); 7.06 (dd, 1H, $H_{5'}$, $J_{5',6'}$= 15 Hz, $J_{5',4'}$= 4 Hz); 6.33 (dd, 1H, $H_{6'}$, $J_{5',6'}$= 15 Hz, $J_{6',4'}$= 1 Hz); 6.2 (d, 1H, $H_{1'}$, $J_{1'2'}$= 0.75 Hz); 5.55 (dd, 1H, $H_{2'}$, $J_{2',3'}$= 6 Hz, $J_{1',2'}$= 0.75 Hz); 5.26 (dd, 1H, $H_{3'}$, $J_{3',2'}$= 6 Hz, $J_{3',4'}$= 3.75 Hz); 4.91 (m, 1H, $H_{4'}$, $J_{4',5'}$= 4 Hz, $J_{4',6'}$= 1 Hz, $J_{4',3'}$= 3.75 Hz); 1.61, 1.4 (2s, 6H, CMe_2).

(Methyl 5',6'-dideoxy-2',3'-O-isopropylidene-6'-(2'-thiopyridyl)-β-D-ribo-hexofuranuronate)-1-Uracil 36

Acid **35** (0.298, 0.5 mmol.) and methyl acrylate (5 eq.) were used. The adduct **36** was isolated as crystals (0.369 g, 82%) (chromatographed: hexane-ethyl acetate, 3.5, 6.5). Anal. Calc. for $C_{20}H_{23}N_3O_7S$. C(53.45); H(5.12); N(9.35); S(7.12). Found: C(53.38); H(5.17); N(9.56); S(7.37); mp: 88-90°C (CH_2Cl_2-ether-pentane). IR: ν_{max} (nujol): 1710, 1690, 1630, 1578, 1416, 1271,1088 cm^{-1}. MS (C.I., m/z): 450 $(MH)^+$; 341 $(MH\text{-}Spy+H)^+$; 113 $(Base+H)^+$; 112 $(Spy+H)^+$.

(Methyl 5',6'-dideoxy-2',3'-O-isopropylidene-6'-β-D-ribo-5'-ene-hexofuranuronate)-1-Uracil 37

0.3 g (0.66 mmol) of addition product **36** was used. The unsaturated ester **37** was isolated as crystals (0.13. g, 60%) (chromatographed: hexane-ethyl acetate, 2.5-7.5); mp 98-100°C (CH_2Cl_2-pentane); lit. 70-72°C. $[\alpha]_D^{20}$= + 51.5 (c= 1; $CHCl_3$); lit. $[\alpha]_D^{20}$= + 47 (c= 1.3; $CHCl_3$); $[\alpha]_D^{20}$= +24 (c= 0.5; DMF). ^1H RMN (200 MHz, $CDCl_3$): δ ppm: 9.96 (s, 1H, NH); 7.26 (d, 1H, H_6, $J_{6,5}$= 8 Hz); 7.00 (dd, 1H, $H_{5'}$, $J_{5',6'}$= 16 Hz, $J_{5',4'}$= 5,5 Hz); 6.05 (dd, 1H, $H_{6'}$, $J_{6',5'}$= 16 Hz, $J_{6',4'}$= 1 Hz); 5.78 (d, 1H, H_5, $J_{5,6}$= 8 Hz); 5.66 (d, 1H, $H_{1'}$, $J_{1',2'}$= 1 Hz); 5.11 (dd, 1H, $H_{2'}$, $J_{2',3'}$= 6 Hz, $J_{2',1'}$= 1 Hz); 4.90 (dd, 1H, $H_{3'}$, $J_{3',2'}$= 6 Hz, $J_{3',4'}$= 5 Hz); 4.66 (t, 1H, $H_{4'}$, $J_{4',3'}$= 5 Hz, $J_{4',5'}$= 5,5 Hz); 3.75 (s, 3H, CO_2CH_3); 1.58, 1.36 (2s, 6H, CMe_2).

(5',6'-Dideoxy-2',3'-O-isopropylidene-6'-phenylsulphonyl-6'-(2'-thiopyridyl)-β-D-ribo-hexofuranosyl)-1-Uracil 38

Acid **35** (0.298, 1 mmol.) and phenyl vinyl sulphone (5 eq.) were used. The adduct **38** was isolated as crystals (0.505 g, 95%) (chromatographed: hexane-ethyl acetate, 3-7). Anal. Calc. for $C_{24}H_{25}N_3O_7S_2$. C(54.23); H(4.70); N(7.90); S(12.05). Found: C(54.06); H(4.67); N(8.15); S(12.23); mp: 106-108°C (CH_2Cl_2-hexane). IR: ν_{max} (nujol): 1685, 1580, 1420, 1310, 1270, 1150, 1080, 760, 720, 690 cm^{-1}. MS (C.I., m/z): 532 $(MH)^+$.

(5',6'-Dideoxy-2',3'-O-isopropylidene-6'-phenylsulphonyl-β-D-ribo-6'-ene-hexofuranosyl)-1-Uracil 39

0.427 g (0.8 mmol) of addition product **38** was used. The olefin **39** was isolated as crystals (0.202 g, 60%) (chromatographed: hexane-ethyl acetate, 3, 7). Anal. Calc. for $C_{19}H_{20}N_2O_7S$. C(54.28); H(4.76); N(6.66); S(7.61). Found: C(54.41); H(5.00); N(6.43); S(7.64). $[\alpha]_D^{20}$= + 64 (c= 0.5; $CHCl_3$).$[\alpha]_D^{20}$= +49 (c= 0.5; DMF); mp 111-114°C (CH_2Cl_2-hexane). IR: ν_{max} (nujol): 1690, 1460, 1380 cm^{-1}. MS (C.I., m/z): 421 $(MH)^+$. ^{1}H RMN (200 MHz, $CDCl_3$): δ ppm: 7.93, 7.63 (m, 5H, Ph); 7.21 (d, 1H, H_6, $J_{6,5}$= 8 Hz); 7.13 (dd, 1H, $H_{5'}$, $J_{5',6}$= 15 Hz, $J_{5',4'}$= 4 Hz); 6.53 (dd,1H, $H_{6'}$, $J_{6',5'}$= 15 Hz, $J_{6',4'}$= 1.5 Hz); 5.76 (d, 1H, H_5, $J_{5,6}$= 8 Hz); 5.58 (s, 1H, $H_{1'}$); 5.20 (d, 1H, $H_{2'}$, $J_{2',3'}$= 6 Hz); 5.00 (dd, 1H, $H_{3'}$, $J_{3',2'}$= 6 Hz, $J_{3',4'}$= 4 Hz); 4.76 (td, 1H, $H_{4'}$, $J_{4',3'}$= $J_{4',5'}$= 4 Hz, $J_{4',6'}$= 1.5 Hz); 1.56, 1.36 (2s, 6H, 2 CMe_2).

(tert-Butyl-3'-O-benzyl-3'-deoxy-β-D-ribo-furanuronate)-1-thymine 40

A solution of CrO_3 (4.8 g, 48 mmol.) and pyridine (7.74 ml, 175 mmol.) in dichloromethane-dimethylformamide (4:1, 120 ml) was stirred at room temperature for 15 min. To this mixture was added a solution of 3'-*O*-benzylthymidine[12] (3.984 g, 12 mmol.) in dichloromethane-dimethylformamide (4:1, 24 ml), acetic anhydride (9 ml, 48 mmol.) and tert-butanol (22.5 ml, 240 mmol.). The reaction mixture was stirred at room temperature for 16h and ethanol was added (6 ml). This solution was diluted with ethyl acetate and filtered through a celite and sodium sulphate pad. The filtrate was evaporated under reduced pressure and the residue was chromatographed on a silica gel column (hexane-ethyl acetate, 6-4) to yield the tert-butylester **40** as crystals (3.376 g, 70%). Anal. Calc. for $C_{21}H_{26}N_2O_6$. C(62.68); H(6.46); N(6.90); Found: C(62.58); H(6.59); N(6.95); mp: 156-158°C (CH_2Cl_2-hexane). $[\alpha]_D^{20}$= + 38 (c= 1; $CHCl_3$). MS (C.I., m/z): 403 $(MH)^+$. ^{1}H RMN (400 MHz, $CDCl_3$): δ ppm: 7.37 (m, 5H, Ph); 7.35 (s, 1H, H_6); 6.52 (dd, 1H, $H_{1'}$, $J_{1'2'}$= 5.25 Hz, $J_{1',2'}$= 9.25 Hz); 4,60 (q, 1H, O$\underline{CH_2}$Ph); 4.58 (s, 1H, $H_{4'}$); 4.20 (d, 1H, $H_{3'}$, $J_{3'2''}$= 5 Hz); 2.52 (dd, 1H, $H_{2'}$, $J_{2'1}$= 5.25 Hz, $J_{2'2''}$= 13;5 Hz); 1.98 (s, 3H, CH_3), 1.9 (m, 1H, $H_{2''}$, $J_{2''3'}$= 5 Hz, $J_{2''1'}$= 9.25 Hz, $J_{2''2'}$= 13.5 Hz); 1.5 (s, 9H, C[CH_3]$_3$).

(3'-O-Benzyl-3'-deoxy-β-D-ribo-furanuronic acid)-1-thymine 41

To a solution of ester **40** (2.6 g, 6.5 mmol.) in dichloromethane (10 ml) trifluoroacetic acid (10 ml) was added. The solution was stirred at 0°C for 3h and evaporated under reduced pressure and then co-evaporated with toluene to afford the crystalline acid **41** (2.14 g, 95%). Anal. Calc. for $C_{17}H_{18}N_2O_6$. C(58.95); H(5.20); N(8.09). Found: C(58.79); H(5.27); N(8.25). mp 238-240°C (methanol). $[\alpha]_D^{20}$= +28 (c= 1; DMF). MS (C.I., m/z): 347 $(MH)^+$. IR ν_{max} (nujol): 3170, 1707, 1656, 1627, 1277, 1245, 1095, 733 cm-1. ^{1}H RMN (400 MHz, $CDCl_3$): δ ppm: 11.48 (s, 1H, COOH); 8.13 (s, 1H, H_6); 7.48 (s, 5H, Ph); 6.42 (dd, 1H, $H_{1'}$, $J_{1',2'}$=9 Hz, $J_{1'2''}$= 5.5 Hz); 4.77 (s, 1H, H4'); 4.72 (q, 2H, $\underline{CH_2}$Ph); 4.52 (d, 1H, $H_{3'}$, $J_{3',2'}$= 5 Hz); 2.5 (dd, 1H, $H_{2''}$, $J_{2'',1'}$= 5.5 Hz, $J_{2'',2'}$= 14 Hz); 2.2 (m, 1H, $H_{2'}$, $J_{2',3'}$= 5 Hz, $J_{2',2''}$= 14 Hz); 1.91 (s, 3H, CH_3).

(3'-O-Benzyloxy-6'-phenylsulphonyl-6'-(2'thiopyridyl)-2',5',6'-trideoxy-β-D-ribo-hexofuranosyl)-1-thymine and 42 {3'-O-Benzyloxy-6'-phenylsulphonyl-6'-(2'thiopyridyl)-2',5',6'-trideoxy-β-L-ribo-hexofuranosyl)-1-thymine 44

Acid **41** (0.346, 1 mmol.) and phenyl vinyl sulphone (5 eq.) were used. The adduct **42** was isolated as crystals (0.350 g, 60%) (chromatographed, hexane-ethyl acetate, 4-6). Anal. Calc. for $C_{29}H_{29}N_3O_6S_2.1/2H_2O$ C(59.18); H(5.10); S(10.88). Found: C(58.98); H(5.22); S(10.93); mp: 90-92°C (CH_2Cl_2-pentane). IR: ν_{max} (nujol): 1690, 1590 cm^{-1}. MS (C.I., m/z): 580 $(MH)^+$

The second product was chromatographed (hexane-ethyl acetate, 3-7) yielding the crystalline **44** (0.058 g, 10%). Anal. Calc. for $C_{29}H_{29}N_3O_6S_2$ C(60.10); H(5.00). Found: C(59.98); H(5.04). mp: 104-106°C (CH_2Cl_2-pentane). IR: ν_{max} (nujol): 1689, 1586, 1463, 1305, 1147, 1083 cm^{-1}. MS (F.A.B., m/z): 580 $(MH)^+$, 127 (base+H).

(3'-O-Benzyloxy-6'-phenylsulphonyl-2',5',6'-trideoxy-β-D-ribo-5'-ene-hexofuranosyl)-1-thymine 43

0.280 g (0.48 mmol) of addition product **42** was used. The unsaturated sulphone **43** was isolated as crystals (0.182 g, 81%) (chromatographed: hexane-ethyl acetate, 4-6). Anal. Calc. for $C_{24}H_{24}N_2O_6S$. C(61.53); H(5.12); N(5.98); S(6.83). Found: C(61.66); H(5.18); N(6.04); S(6.85).$[\alpha]_D^{20}$= +81 (c= 0.5; $CHCl_3$) $[\alpha]_D^{20}$= +52 (c= 0.5; DMF); mp: 161-163°C (CH_2Cl_2-ether). IR: ν_{max} (nujol): 1709, 1686, 1464, 1295, 1142, 1083, 739 cm^{-1}. MS (C.I., m/z): 469 $(MH)^+$. ^1H RMN (200 MHz, $CDCl_3$): δ ppm: 9.03 (s, 1H, NH) 7.86, 7.56, 7,33 (m, 10H, Ph); 7.05 (dd, 1H, $H_{5'}$, $J_{5',4'}$= 4 Hz, $J_{5',6'}$= 15 Hz); 6.98 (s, 1H, H_6); 6.60 (dd, 1H, $H_{6'}$, $J_{6',5'}$= 15 Hz, $J_{6',4'}$= 1.75 Hz); 4.61 (td, 1H, $H_{4'}$, $J_{4',5'}$= 4 Hz, $J_{4',3'}$= 4 Hz, $J_{4',6'}$= 1.75 Hz); 4.56 (q, 2H, O<u>CH_2</u>Ph); 4.15 (m, 1H, $H_{3'}$, $J_{3',4'}$= 4 Hz, $J_{3',2'}$= 7 Hz, $J_{3',2''}$= 3.5 Hz); 2.43 (m, 1H, $H_{2''}$, $J_{2'',2'}$= 14 Hz, $J_{2'',3'}$= 3.5 Hz, $J_{2'',1}$= 6.5 Hz); 2.16 (m, 1H, $H_{2'}$, $J_{2',2''}$= 14 Hz, $J_{2',3'}$= $J_{2',1'}$= 7 Hz); 1.83, 1.78 (2s, 3H, CH_3).

(3'-O-Benzyloxy-6'-phenylsulphonyl-2',5',6'-trideoxy-β-L-ribo-5'-ene-hexofuranosyl)-1-thymine 45

0.047 g (0.08 mmol) of addition product **44** was used. The unsaturated sulphone **45** was isolated as crystals (0.028 g, 75%) (chromatographed: hexane-ethyl acetate, 3-7). Anal. Calc. for $C_{24}H_{24}N_2O_6S$ 1/2H_2O. C(60.37); H(5.24). Found: C(60.39); H(5.34). $[\alpha]_D^{20}$= +15 (c= 0.5; DMF); mp: 84-86°C (CH_2Cl_2-pentane). IR: ν_{max} (nujol): 1689, 1146 cm^{-1}. MS: (C.I., m/z): 469 $(MH)^+$. ^1H RMN (200 MHz, $CDCl_3$): δ ppm: 9.06 (s, 1H, NH) 7.86, 7.33 (m, 10H, Ph); 7.05 (s, 1H, H_6); 7.03 (dd, 1H, $H_{5'}$, $J_{5',4'}$= 4 Hz, $J_{5',6'}$= 15 Hz); 6.68 (dd, 1H, $H_{6'}$, $J_{6',5'}$= 15 Hz, $J_{6',4'}$= 1.5 Hz); 6.08 (t, 1H, $H_{1'}$, $J_{1'2}$= 6.75); 5.06 (td, 1H, $H_{4'}$, $J_{4',5'}$= 4 Hz, $J_{4',3'}$= 4 Hz); 4.5 (q, 2H, O<u>CH_2</u>Ph); 4.41 (m, 1H, $H_{3'}$); 2.65 (dd, 1H, $H_{2'}$, $J_{2',2''}$= 13 Hz, $J_{2''}$, $_{3'}$= 6.5 Hz, $J_{2'',1'}$= 6.5 Hz); 2.33 (m, 1H, $H_{2''}$, $J_{2'',2'}$= 13 Hz, $J_{2'',3'}$= 5 Hz, $J_{2',1'}$= 7 Hz); 1.91 (s, 3H, CH_3).

(3'-O-tert-Butyldiphenylsilyl-6'-phenylsulphonyl-6'-(2'-thiopyridyl)-2',5',6'-trideoxy-β-D-ribo-hexofuranosyl)-1-thymine 47 and {3'-O-tert-butyldiphenylsilyl-6'-phenylsulphonyl-6'-(2'-thiopyridyl)-2',5',6'-trideoxy-β-L-ribo-hexofuranosyl)-1-thymine 48

Acid **46** (0.494, 1 mmol.) and phenyl vinyl sulphone (5 eq.) were used. The adduct **47** was isolated as crystals (0.525 g, 72%) (chromatographed: hexane-ethyl acetate, 6-4). Anal. Calc. for $C_{38}H_{41}N_3O_6S_2$ Si C(62.72); H(5.63); N(5.77); S(8.80). Found: C(62.63); H(5.72); N(5.66); S(8.62); mp: 104-110°C (ether-pentane). MS (F.A.B., m/z): 728 $(MH)^+$.

A second elution using hexane-ethyl acetate: 4.5, 5.5 gave the crystalline **48** (0.029 g, 4%). Anal. Calc. for $C_{38}H_{41}N_3O_6S_2$ Si C(62.72); H(5.63); N(5.77); S(8.80). Found: C(62.53); H(5.70); N(5.54); S(8.65); mp: 104-110°C (ether-pentane). MS (F.A.B., m/z): 728 $(MH)^+$.

(3'-O-tert-Butyldiphenylsilyl-6'-phenylsulphonyl-2',5',6'-trideoxy-β-D-ribo-5'-ene-hexofuranosyl)-1-thymine 49

0.364 g (0.5 mmol) of addition product **47** was used. The unsaturated sulphone **49** was isolated as crystals (0.201 g, 65%) (chromatographed: hexane-ethyl acetate, 6-4). Anal. Calc. for $C_{33}H_{36}N_2O_6S$ Si. C(64.28); H(5.84); N (4.54); S(5.19). Found: C(64.08); H(5.87); N (4.68); S(5.18). $[\alpha]_D^{20}$= +44 (c= 0.5; $CHCl_3$); $[\alpha]_D^{20}$= +28 (c= 0.5; DMF); mp: 92-96°C (ether-pentane). IR: ν_{max} (nujol): 1692, 1320, 1308, 1148, 1112, 1085, 703 cm^{-1}. MS (C.I., m/z): 617 $(MH)^+$. ^{1}H RMN (400 MHz, $CDCl_3$): δ ppm: 8.53 (s, 1H, NH) 7.8, 7.42 (m, 15H, Ph); 6.83 (s, 1H, H_6); 6.60 (dd, 1H, $H_{5'}$, $J_{5',4'}$= 4 Hz, $J_{5',6'}$= 15 Hz); 6.45 (dd, 1H, $H_{1'}$, $J_{1',2'}$= 7 Hz, $J_{1',2''}$= 6 Hz); 6.26 (dd, 1H, $H_{6'}$, $J_{6',5'}$= 15 Hz, $J_{6',4'}$= 1.5 Hz); 4.46 (m, 1H, $H_{4'}$, $J_{4',5'}$= 4 Hz, $J_{4',3'}$= 3 Hz, $J_{4',6'}$= 1.5 Hz); 4.26 (m, 1H, 1H, $H_{3'}$, $J_{3',2'}$= 6 Hz, $J_{3',2''}$= $J_{3',4'}$= 3 Hz); 2.32 (qd, 1H, $H_{2''}$, $J_{2'',2'}$= 14 Hz, $J_{2'',3'}$= 3 Hz, $J_{2'',1'}$= 6 Hz); 1.86 (td, 1H, $H_{2'}$, $J_{2',2''}$= 14 Hz, $J_{2',3'}$= 6 Hz, $J_{2',1'}$= 7 Hz); 1.83 (s, 3H, CH_3); 1.08 (s, 9H, $[CH_3]_3CSi$).

(3'-O-tert-Butyldiphenylsilyl-6'-phenylsulphonyl-2',5',6'-trideoxy-β-L-ribo-5'-ene-hexofuranosyl)-1-thymine 50

0.030 g (0.04 mmol) of addition product **48** was used. The unsaturated sulphone **50** was isolated as crystals (0.018 g, 70%) (chromatographed: hexane-ethyl acetate, 1-1). HRMS: Calc. 617.2141; found: 617.2136. $[\alpha]_D^{20}$=+17 (c= 1; $CHCl_3$); mp: 118-120°C (CH_2Cl_2-hexane). IR: ν_{max} (nujol): 1708, 1692, 1320, 1148, 1112, 1086, 708 cm^{-1}. MS (C.I., m/z): 617 $(MH)^+$. ^{1}H RMN (400 MHz, $CDCl_3$): δ ppm: 8.76 (s, 1H, NH) 8-7.56 (m, 15H, Ph); 7.03 (dd, 1H, $H_{5'}$, $J_{5',4'}$= 4 Hz, $J_{5',6'}$= 15 Hz); 6.96 (s, 1H, H6); 6.71 (dd, 1H, $H_{6'}$, $J_{6',5'}$= 15 Hz, $J_{6',4'}$= 1.5 Hz); 6.33 (t, 1H, $H_{1'}$, $J_{1',2''}$= 7 Hz, $J_{1',2''}$= 7 Hz); 4.86 (m, 1H, $H_{4'}$); 4.63 (m, 1H, $H_{3'}$); 2.21 (m, 1H, $H_{2'}$); 2.03 (m, 1H, $H_{2''}$); 1.86 (s, 3H, CH_3); 1.08 (s, 9H, $[CH_3]_3CSi$).

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