Synthesis of Spiro[1,4-benzothiazine-2,2'-pyrans] Starting from Methyl β-D-*arabino*-2-Hexulopyranosonate

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Dedicated to Professor Klaus Burger on the occasion of his 60th birthday

Methyl β-D-*arabino*-2-hexulopyranosonate **1** has *via* the novel glycosyl donor **3** been transformed into the thiophenyl glycosides **4** and **5**. Catalytic hydrogenation of the nitro compound **4** in alkaline solution led to spontaneous cyclization and deprotection to form the cyclic hydroxamic acid **7**. The related lactams **8** and **9** were obtained from amine **5**. The spiro[1,4-benzothiazine-2,2'-pyrans] **7-9** are the first representatives of a novel class of heterocycles structurally related to bioactive natural products. As shown by the values for $J_{3',4'}$ and $J_{4',5'}$ the glycosides **4**, **5** and **6** adopt a $^5C_2$ conformation of the pyranoid ring whereas the 1,4-benzothiazine system in **7-9** forces a conformational change into the $^2C_5$ conformation.

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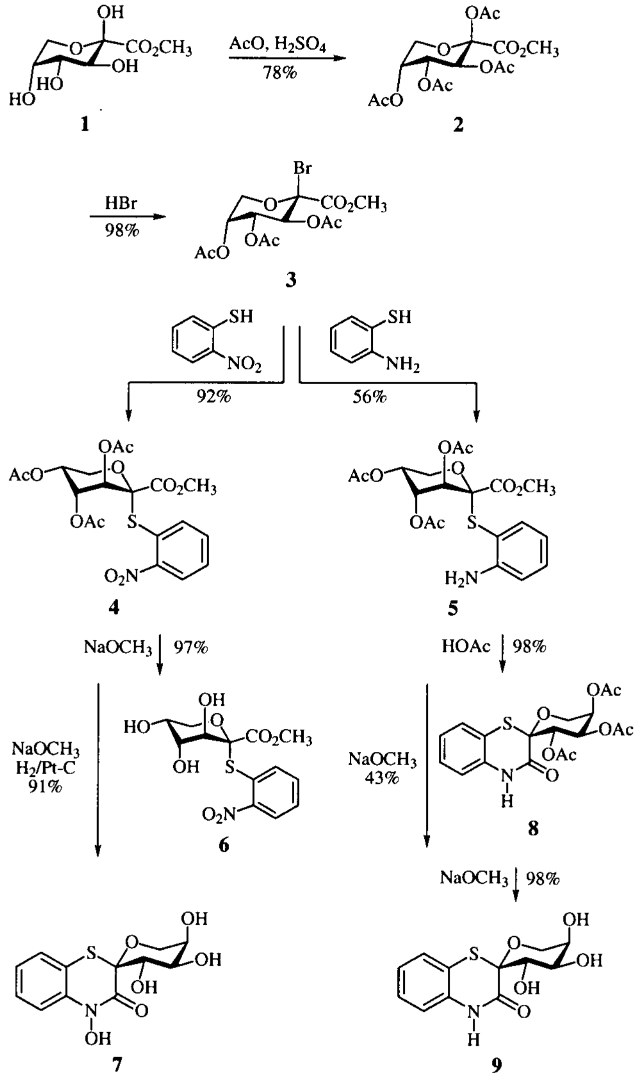
Though D-*arabino*-2-hexulosonic acid (2-oxo-D-gluconic acid) is used on industrial scale for the production of D-isoascorbic acid [1], it has hitherto received little attention for synthetic applications [2,3]. We have reported on the synthesis of D-*arabino*-2-hexulosonic acid both by fermentation of D-glucose with *Serratia marcescens* and an optimized oxidation of 2,3:4,5-di-*O*-isopropylidene-D-fructose with potassium permanganate [4]. Esterification led to the crystalline methyl β-D-*arabino*-2-hexulopyranosonate **1** as a suitable starting material for the synthesis of compounds related to two classes of natural products. Hence, naturally occurring heterocyclic spiranes are of interest due to their biological activity. Thus, spiroacetalic papulacandins [5], fruit fly pheromones [6], the herbicide (+)-hydantocidin [7] and its analogues which have been found to inhibit the glycogen phosphorylase [8], or gelsemium [9] and triticum alkaloids [10] have been reported. On the other hand, certain natural benzoxazinoids exhibit high bioactivity as plant own resistance factors against microbial diseases and insects, as allelo chemicals and endogeneous ligands and are of synthetic interest [11]. Thus, we have described both the synthesis of natural occurring benzoxazinone acetal glucosides [12], their hemiacetalic aglucones [13] and of aza and thio analogues [14,15].

We wish to report here on the synthesis of substituted thiophenyl glycosides of D-*arabino*-2-hexulosonic acid and there cyclization to form spiro[1,4-benzothiazine-2,2'-pyrans] as representatives of a novel class of heterocycles which is in relationship to the natural products mentioned.

Results and Discussion.

On reinvestigating the acetylation of methyl β-D-*arabino*-2-hexulopyranosonate **1** with acetic anhydride [16,17] we have found that this reaction in the presence of sulfuric acid as catalyst afforded methyl 2,3,4,5-tetra-*O*-acetyl-α-D-*arabino*-2-hexulopyranosonate **2** as main product in 78% yield.



Bromination of **2** with a solution of hydrogen bromide in glacial acetic acid resulted in the crystalline methyl 2-bromo-3,4,5-tri-*O*-acetyl-α-D-*arabino*-2-hexulopyranosonate **3**, nearly quantitatively. Reaction of glycosyl donor **3** with potassium 2-nitro- and 2-aminothiophenolate gave rise to methyl 2-*S*-(2-nitrophenyl)-3,4,5-tri-*O*-acetyl-α-D-*arabino*-2-hexulopyrano-sonate **4** and methyl 2-*S*-(2-aminophenyl)-3,4,5-tri-*O*-acetyl-α-D-*arabino*-2-hexulopyranosonate **5**. Due to the neighbouring group assistance of the 3-acetyl group this reaction proceeds with inversion of the configuration at the anomeric centre *via* an intermediate acetyl oxonium ion, in which the axial position is shielded. Therefore, a nucleophile can only attack from the equatorial direction which leads to an inversion at the anomeric centre. Hence, diastereoselectively the 2,3-trans configurated glycosides **4** and **5** are obtained, exclusively. Catalytic hydrogenation of nitro compound **4** in methanol over platinum on carbon at normal pressure gave also rise to methyl 2-*S*-(2-aminophenyl)-3,4,5-tri-*O*-acetyl-α-D-*arabino*-2-hexulo-pyranosonate **5**, which did not cylize under these conditions. However, on treatment with glacial acetic acid **5** cyclized to form (2*S*)-3',4',5'-tri-*O*-acetyl-D-*arabino*-2*H*-1,4-benzothiazine-2-spiro-2'-pyran-3(4*H*)-one **8** as a lactam. Compound **8** was deprotected to yield (2*S*)-3',4',5'-trihydroxy-D-*arabino*-2*H*-1,4-benzothiazine-2-spiro-2'-pyran-3(4*H*)-one **9**. Similar to the deprotection protocol for **8**, in a one pot procedure **5** was in the presence of sodium methanolate in methanol cyclized and deprotected to form **9**, but with an insufficient yield in comparison to the two step method *via* the triacetate **8**. However, in contrast to **5**, when glycoside **4** was treated with sodium methanolate in methanol methyl 2-*S*-(2-nitrophenyl)-α-D-*arabino*-2-hexulopyranosonate **6** was obtained as expected.

Due to the cyclic hydroxamic acid feature occurring in many of the natural benzoxazinone glucosides we have been especially interested in a synthetic access to the cyclic hydroxamic acid analogue of lactam **9**. Finally, this aim led to an unconventional approach to (2*S*)-3',4,4',5'-tetrahydroxy-D-*arabino*-2*H*-1,4-benzothiazine-2-spiro-2'-pyran-3(4*H*)-one **7**. Hydrogenations under strongly basic conditions are unusual but not impossible. Therefore, we have subjected nitro compound **4** to a catalytic hydrogenation in methanol containing sodium methanolate over platinum on carbon at normal pressure. This method ensured spontaneous cyclization of the hydroxylamine intermediate formed during reduction and deprotection at the same time and afforded the cyclic hydroxamic acid **7** in very good yield.

The structures of compounds **2-9** were assigned by spectroscopic methods. Interesting findings were obtained on the conformation of the pyranoid ring in compounds **4-9**. If a ${}^2C_5$ or a ${}^5C_2$ conformation is favoured results from the interactions of the substituents at positions C-3'and C-4' of the saccharidic moiety with the thiophenyl substituent at C-2' or the spiro connected 1,4-benzothiazinone ring, respectively.

The glycosides **4**, **5** and **6** adopt a ${}^5C_2$ pyranoid ring conformation with an axial anomeric substituent and equatorially oriented methyl carboxylate group indicated by the small ^{1}H nmr coupling constants ($J_{3,4}$ 3.7-4.4, $J_{4,5}$ 3.3-3.4 Hz). The 1,4-benzothiazine system of the cyclization products **7-9** forced a conformational change into the ${}^2C_5$ conformation indicated by the increasing values for the $H_{3'}$-$H_{4'}$-coupling constant ($J_{3',4'}$ 7.7-8.4, $J_{4',5'}$ 3.5-3.7 Hz).

In summary, we have based on methyl β-D-*arabino*-2-hexulopyranosonate **1** *via* the thiophenyl glycosides **4** and **5** synthesized the cyclic hydroxamic acid **7** and the lactams **8** and **9** as first representatives of the spiro[1,4-benzothiazine-2,2'-pyrans], a novel class of heterocycles structurally related to bioactive natural products.

EXPERIMENTAL

Melting points were measured on a Boetius micro hot-stage and are corrected. The ir spectra were obtained on a Carl Zeiss Jena spectrometer M80 in potassium bromide. The nmr spectra were recorded with a Varian Gemini 200 (^{1}H, 199.975 MHz; ^{13}C, 50.289 MHz) or Varian Unity 400 (^{1}H, 399.97552 MHz) with hexamethyldisiloxane as the internal standard. Mass spectra were recorded on a VG Masslab Manchester VG 12-250 spectrometer (70 eV EI ionisation). Optical rotations were determined with a semiautomatic polarimeter Polartronic-D (Schmidt & Haensch) using the Na-D line. The tlc were performed on precoated Silica gel 60 F_{254} aluminum sheets (Merck), spots were visualized by gentle heating. Silica gel 60 (0.063-0.200 mm) (Merck) was used for column chromatography. Elemental analyses were performed on a Heraeus CHN-O-Rapid analyzer. Crystalline methyl β-D-*arabino*-2-hexulopyranosonate **1** was prepared from a fermentation solution containing D-*arabino*-2-hexulopyranosonic acid and sodium D-*arabino*-2-hexulopyranosonate according to our published method [4].

Methyl 2,3,4,5-Tetra-*O*-acetyl-β-D-*arabino*-2-hexulopyranosonate (**2**).

To a stirred suspension of **1** (4.16 g, 20 mmoles) in acetic anhydride (25 ml) concentrated sulfuric acid (0.5 ml) was added at 20°. The temperature raised to 60° and was kept there for 20 minutes. The solution was cooled then and poured into ice. The precipitate was filtered off, washed with water and recrystallized from MeOH to yield 5.86 g (78%) of colourless crystals of **2**, mp 171°, (lit. 168-169° [17]); $[\alpha]_D^{22}$-130° (c 1.0, chloroform); ir: ν 1750 CO, 1630 CO cm^{-1}; ^{1}H nmr (400 MHz, deuteriochloroform): δ 2.01 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.18 (s, 3H, CH_3), 2.21 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 3.90 (d, 1H, $J_{6a,b}$ = 13.4 Hz, H_{6a}), 4.02 (d, 1H, $J_{6a,b}$ = 13.4 Hz, H_{6b}), 5.38 (m, 1H, H_4), 5.39 (m, 1H, H_5), 5.45 (d, 1H, $J_{3,4}$ = 10.4 Hz, H_3); ^{13}C nmr (deuteriochloroform): δ 20.9 (CH_3), 21.0 (CH_3), 21.2 (CH_3), 21.3 (CH_3), 53.9 (OCH_3), 63.9 (C-6), 67.1 (C-5), 68.9 (C-4), 67.9 (C-3), 96.5 (C-2), 165.3 (C-1), 168.6 (CO), 170.2 (CO), 170.3 (CO), 170.7 (CO); ms: m/z 317 (M^+, 37), 275 (11), 257 (5), 233 (7), 216 (10), 197 (16), 170 (40), 155 (19), 128 (40), 115 (18), 43 (100).

Methyl 2-Bromo-3,4,5-tri-*O*-acetyl-β-D-*arabino*-2-hexulopyranosonate (**3**).

A mixture of powdered **2** (3.76 g, 10 mmoles) in a 33% solution of hydrogen bromide in glacial acetic acid (40 ml) was stirred for 2 hours at 20°. The solution was diluted with cold chloroform (60 ml) and poured into ice water (100 ml). The chloroform layer was separated and the aqueous phase extracted again with chloroform (15 ml).

The chloroform extracts were washed successively with ice water (60 ml), twice with a cold 2 % solution of sodium hydrogencarbonate (2 x 60 ml) and again with ice water (60 ml). After drying the colourless solution over magnesium sulfate the solvent was evaporated *in vacuo* to yield 3.89 g (98%) of a colourless powder of **3**, mp 78-80°; $[\alpha]_D^{20}$ -175° (c 1.0, chloroform); ir: ν 1750 CO cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 2.00 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 2.15, (s, 3H, CH_3), 3.85 (s, 3H, OCH_3), 4.33 (d, 1H, $J_{6a,b}$ = 13.4 Hz, H_{6a}), 4.25 (d, 1H, $J_{6a,b}$ = 13.4 Hz, H_{6b}), 5.39 (m, 1H, H_5), 5.13 (dd, 1H, $J_{3,4}$ = 10.0, $J_{4,5}$ = 3.2 Hz, H_4), 5.48 (d, 1H, $J_{3,4}$ = 10.0 Hz, H_3); ^{13}C nmr (deuteriochloroform): δ 21.0 (CH_3), 21.3 (CH_3), 21.3 (CH_3), 54.4 (OCH_3), 66.9 (C-6), 67.4 (C-5), 67.7 (C-4), 69.9 (C-3), 95.9 (C-2), 165.5 (C-1), 169.5 (CO), 170.3 (CO), 170.5 (CO); ms: m/z 356 δ (M^+ + 2) - CH_3CO), 8), 354 (M^+ - CH_3CO), 9), 317 (20, M^+ - HBr), 259 (12), 197 (17), 173 (23), 155 (39), 128 (37), 43 (100).

Anal. Calcd. for $C_{13}H_{17}BrO_9$: C, 39.31; H, 4.31. Found: C, 39.66; H, 4.16.

General Procedure for the Glycosidation to Form the Glycosides **4** and **5**.

To a solution of **3** (1.19 g, 3.0 mmoles) in dry acetone (25 ml) were added 3.1 mmoles of the corresponding pure thiophenol (0.48 g of 2-nitrothiophenol for **4**; 0.39 g of 2-aminothiophenol for **5**) and potassium carbonate (0.83 g, 6.0 mmoles). After refluxing for 2 hours under a nitrogen atmosphere chloroform (15 ml) was added and the mixture was cooled to 0°. The resultant potassium bromide was filtered and washed with chloroform. The filtrate was evaporated *in vacuo*. The resulting syrup was purified by column chromatography with toluene/ethyl acetate (2:1, v/v).

Methyl 2-*S*-(2-Nitrophenyl)-3,4,5-tri-*O*-acetyl-α-ᴅ-*arabino*-2-hexulopyranosonate (**4**).

The product fraction was evaporated *in vacuo* and the homogeneous residue recrystallized from methanol to yield 1.30 g (92%) of pale yellow crystals of **4**, mp 54-56°; $[\alpha]_D^{22}$ + 225° (c 1.0, chloroform); ir: ν 1750 CO, 1530 NO_2, 1370 NO_2 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 2.01 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 3.49 (s, 3H , OCH_3), 4.09 (dd, 1H, $J_{6a,6b}$ = 11.2, $J_{5,6a}$ = 4.8 Hz, H_{6a}), 4.45 (dd, 1H, $J_{6a,6b}$ = 11.2, $J_{5,6b}$ = 9.9 Hz, H_{6b}), 5.28 (ddd, 1H, $J_{5,6a}$ = 9.8, $J_{5,6b}$ = 4.8, $J_{4,5}$ = 3.3 Hz, H_5), 5.34 (dd, 1H, $J_{3,4}$ = 4.4, $J_{4,5}$ = 3.3 Hz, H_4), 5.51 (d, 1H, $J_{3,4}$ = 4.4 Hz, H_3), 7.47 (dd, 1H, $J_{5,6}$ = 8.0, $J_{4,5}$ = 7.5 Hz, $H_{5'}$), 7.55 (dd, 1H, $J_{3,4}$ = 8.0, $J_{4,5}$ = 7.5 Hz, $H_{4'}$), 7.87 (d, 1H, $J_{3,4}$ = 8.0 Hz, $H_{3'}$), 7.84 (d, 1H, $J_{5,6}$ = 8.0 Hz, $H_{6'}$); ^{13}C nmr (deuteriochloroform): δ 20.9 (CH_3), 21.1 (CH_3), 21.3 (CH_3), 53.3 (OCH_3), 60.2 (C-6), 65.0 (C-5), 66.9 (C-4), 71.4 (C-3), 91.3 (C-2), 125.1 (C-3'), 127.1 (C-1'), 129.7 (C-4'), 132.8 (C-6'), 136.1 (C-5'), 152.6 (C-2'), 166.3 (C-1), 168.4 (CO), 169.6 (CO), 170.0 (CO); ms: m/z 471 M^+ (6), 439 (5), 398 (5), 341 (11), 317 (20), 278 (10), 215 (17), 197 (26), 155 (43), 42 (100).

Anal. Calcd. for $C_{19}H_{21}NO_{11}S$: C, 48.41; H, 4.49; N, 2.97. Found: C, 48.64; H, 4.65; N, 3.05.

Methyl 2-*S*-(2-Aminophenyl)-3,4,5-tri-*O*-acetyl-α-ᴅ-*arabino*-2-hexulopyranosonate (**5**).

Column chromatography gave successively: 0.43 g (36%) of starting compound **3** and 0.74 g (56 %) of colourless crystals of **5**, mp 174-175°; $[\alpha]_D^{22}$ + 158° (c 1.0, chloroform); ir: ν 3400 NH, 1760 CO cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 2.01 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 2.20 (s, 3H, CH_3), 3.44 (s, 3H , OCH_3), 4.05 (dd, 1H, $J_{6a,6b}$ = 10.3, $J_{5,6b}$ = 4.8 Hz, H_{6a}), 4.07-4.30 (s, 2H, NH_2), 4.58 (d, 1H, $J_{6a,6b}$ = 10.3 Hz, H_{6b}), 5.24 (ddd, 1H, $J_{5,6a}$ = 9.5 $J_{5,6b}$ = 4.8, $J_{4,5}$ = 3.3 Hz, H_5), 5.32 (dd, 1H, $J_{3,4}$ = 4.8, $J_{4,5}$ = 3.3 Hz, H_4), 5.66 (d, 1H, $J_{3,4}$ = 4.4 Hz, H_3), 6.67 (m, 1H, $H_{5'}$), 6.69 (d, 1H, $J_{3,4}$ = 7.6 Hz, $H_{3'}$), 7.15 (dd, 1H, $J_{3,4}$ = 7.6, $J_{4,5}$ = 8.1 Hz, $H_{4'}$), 7.29 (d, 1H, $J_{5,6}$ = 7.6 Hz, $H_{6'}$); ^{13}C nmr (deuteriochloroform): δ 20.9 (CH_3), 21.1 (CH_3), 21.3 (CH_3), 53.0 (OCH_3), 60.0 (C-6), 65.2 (C-5), 67.1 (C-4), 71.5 (C-3), 91.9 (C-2), 112.7 (C-3'), 115.9 (C-1'), 118.9 (C-5'), 132.2 (C-4'), 139.2 (C-6'), 150.5 (C-2'), 166.6 (C-1), 168.8 (CO), 169.7 (CO), 170.2 (CO); ms: m/z 441 (M^+, 4), 318 (32), 276 (3), 257 (3), 216 (10), 198 (25), 155 (53), 43 (100).

Anal. Calcd. for $C_{19}H_{23}NO_9S$: C, 51.70; H, 5.25; N, 3.17. Found: C, 51.58; H, 5.56; N, 3.54.

General Procedure for the Deacetylation to Form **6** and **9**.

To a solution of the corresponding acetate (94 mg of **4** for **6**; 81 mg (0.2 mmoles) of **8** for **9**) in dry methanol (2 ml) was added a methanolic solution of sodium methanolate (2 ml, 0.1 *N*). After the solution was stirred for 15 minutes the solution was neutralized by stirring with an ion exchange resin (Amberlite IR 120 (H^+)). The resin was filtered and the filtrate evaporated *in vacuo*.

Methyl 2-*S*-(2-Nitrophenyl)-α-ᴅ-*arabino*-2-hexulopyranosonate (**6**).

Recrystallization of the residue from *n*-hexane/tetrahydrofuran gave 67 mg (97%) **6** as pale yellow crystals, mp 76-77°; $[\alpha]_D^{24}$ + 248° (c 0.5, methanol); ir: ν 3430 OH, 1740 CO, 1530 NO_2, 1360 NO_2 cm^{-1}; ^1H nmr (200 MHz, methanol-d_4): δ 3.39 (s, 3H, OCH_3), 3.78 (dd, 1H, $J_{5,6a}$ = 5.1 Hz, $J_{6a,6b}$ = 10.6 Hz, H_{6a}), 3.95 (dd, 1H, $J_{3,4}$ = 3.7 Hz, $J_{4,5}$ = 3.3 Hz, H_4), 4.08 (ddd, 1H, $J_{4,5}$ = 3.3, $J_{5,6b}$ = 10.7, $J_{5,6a}$ = 5.1 Hz, H_5), 4.27 (d, 1H, $J_{3,4}$ = 3.7 Hz, H_3), 4.40 (dd, 1H, $J_{5,6b}$ = 10.7, $J_{6a,6b}$ = 10.6 Hz, H_{6b}), 7.51 (m, 2H, $H_{4'}$, $H_{5'}$), 7.80 (m, 2H, $H_{3'}$, and $H_{6'}$); ^{13}C nmr (methanol-d_4): δ 53.2 (OCH_3), 62.3 (C-6), 64.7 (C-5), 72.3 (C-4), 75.6 (C-3), 94.7 (C-2), 125.4 (C-3'), 129.7 (C-1'), 130.2 (C-4'), 133.4 (C-6'), 137.3 (C-5'), 154.3 (C-2'), 169.7 (C-1); ms: m/z 286 (M^+ - $COOCH_3$, 23), 222 (3), 191 (27), 174 (82), 154 (25), 132 (50), 119 (43), 58 (100).

Anal. Calcd. for $C_{13}H_{15}NO_8S$: C, 45.22, H, 4.38; N, 4.06. Found: C, 44.98, H, 4.76; N, 4.12.

(2*S*)-3',4',5'-Trihydroxy-ᴅ-*arabino*-2*H*-1,4-benzothiazine-2-spiro-2'-pyran-3(4*H*)-one (**9**).

Recrystallization of the residue from chloroform/methanol (7:3, v/v) gave 55 mg (98%) of colourless needles of **9**, mp 209-211°; $[\alpha]_D^{26}$ + 297° (methanol, c 1.03); ir: ν 3410 NH, OH, 1670 CO cm^{-1}; ^1H nmr (200 MHz, methanol-d_4): δ 3.51 (d, 1H, $J_{6'a,6'b}$ = 12.1 Hz, $H_{6'a}$), 3.79 (d, 1H, $J_{6'a,6'b}$ = 12.1 Hz, $H_{6'b}$), 3.91 (m, 1H, $H_{5'}$), 3.93 (d, 1H, $J_{3',4'}$ = 7.7 Hz, $H_{3'}$), 4.37 (dd, 1H, $J_{3',4'}$ = 7.7, $J_{4',5'}$ = 3.7 Hz, $H_{4'}$), 6.97 (d, 1H, $J_{5,6}$ = 7.9 Hz, H_5), 7.01 (dd, 1H, $J_{7,8}$ = 7.7 Hz, $J_{6,7}$ = 7.5 Hz, H_7), 7.17 (dd, 1H, $J_{5,6}$ = 7.9 Hz, $J_{6,7}$ = 7.5, Hz, H_6), 7.30 (d, 1H, $J_{7,8}$ = 7.7 Hz, H_8); ^{13}C nmr (methanol-d_4): δ 66.9 (C-6'), 68.7 (C-5'), 72.0 (C-4'), 74.1 (C-3'), 83.7 (C-2), 117.9 (C-5), 119.7 (C-8a), 124.9 (C-7), 128.2 (C-6), 129.2 (C-8), 137.0 (C-4a), 165.3 (C-3); ms: m/z 283 (M^+, 17), 192 (2), 180 (100), 151 (56).

Anal. Calcd. for $C_{12}H_{13}NO_5S$: C, 50.88; H, 4.62; N, 4.94. Found: C, 50.78; H, 4.48; N, 5.13.

General Procedure for the Catalytic Hydrogenation of **4** to Form **5** and **7**.

A solution of **4** (0.47 g, 1 mmole) in methanol (15 ml for **5** and **7**) and additional 15 ml of 0.1 *N* sodium methanolate (for **7** only) was hydrogenated over 5% Pt-C (0.10 g) at normal pressure and room temperature until the hydrogen uptake ceased. The catalyst was filtered off and the filtrate evaporated *in vacuo*.

Methyl 2-*S*-(2-Aminophenyl)-3,4,5-tri-*O*-acetyl-α-D-*arabino*-2-hexulopyranosonate (**5**).

Recrystallization of the residue from methanol gave 0.42 g (95%) of colourless needles of **5**, mp 174-175°.

(2*S*)-3',4,4',5'-Tetrahydroxy-D-*arabino*-2*H*-1,4-benzothiazine-2-spiro-2'-pyran-3(4*H*)-one (**7**).

Recrystallization of the residue from methanol gave 0.27 g (91%) of colourless needles of **7**, mp 237-239°; $[\alpha]_D^{26}$ + 180° (c 0.5, methanol/water 3:1, (v/v)); ir: ν 3440-3370 OH, 1650 CO cm^{-1}; ^1H nmr (400 MHz, dimethyl-d_6 sulfoxide): δ 3.36 (d, 1H, $J_{6',6'b}$ = 12.1 Hz, $H_{6'a}$), 3.62 (d, 1H, $J_{6'a,6'b}$ = 12.1 Hz, $H_{6'b}$), 3.76 (m, 1H, $H_{5'}$), 3.81 (dd, 1H, $J_{3',4'}$ = 8.4 Hz, $J_{3',3'-OH}$ =5.8 Hz, $H_{3'}$), 4.27 (ddd, 1H, $J_{3',4'}$ = 8.4 Hz, $J_{4',5'}$ = 3.5 Hz, $J_{4',4'-OH}$ = 5.8 Hz, $H_{4'}$), 4.70 (d, 1H, $J_{5',5'-OH}$ = 4.3 Hz, 5'-OH), 5.04 (d, 1H, $J_{4',4'-OH}$ = 5.8 Hz, 4'-OH), 5.42 (d, 1H, $J_{3',3'-OH}$ = 5.8 Hz, 3'-OH), 7.29 (dd, 1H, $J_{5,6}$ = 7.7 Hz, $J_{6,7}$ = 7.6 Hz, H_6), 7.36 (d, 1H, $J_{5,6}$ = 7.7 Hz, H_5), 7.06 (dd, 1H, $J_{7,8}$ = 8.0 Hz, $J_{6,7}$ = 7.6 Hz, H_7), 7.37 (d, 1H, $J_{7,8}$ = 7.7 Hz, H_8), 10.81 (s, 1H, N-OH) ; ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 66.5 (C-6'), 66.9 (C-5'), 69.6 (C-4'), 72.1 (C-3'), 84.0 (C-2), 114.5 (C-5), 117.2 (C-8a), 123.7 (C-7), 126.9 (C-6), 127.6 (C-8), 137.6 (C-4a), 158.5 (C-3); ms: m/z 299 (M^+, 47), 283 (18), 180 (100), 167 (46), 150 (46).

Anal. Calcd. for $C_{12}H_{13}NO_6S$: C, 48.16; H, 4.38; N, 4.68. Found: C, 48.01; H, 4.71; N, 5.01.

(2*S*)-3',4',5'-Tri-*O*-acetyl-D-*arabino*-2*H*-1,4-benzothiazine-2-spiro-2'-pyran-3(4*H*)-one (**8**).

A solution of **5** (88 mg, 0.2 mmole) in glacial acetic acid (3 ml) was stirred for 2 days. The solvent was evaporated *in vacuo* and the resin recrystallized from n-hexane/methanol 10:1 δ v/v) to give 73 mg (90%) of colourless crystals of **8**, mp 240-241°; $[\alpha]_D^{26}$ + 32° (c 0.5, chloroform); ir: ν 3435 NH, 1750 CO, 1690 CO cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 2.01 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 2.16 (s, 3H, CH_3), 3.91 (m, 2H, $H_{6'a}$, $H_{6'b}$), 5.42 (m, 1H, $H_{5'}$), 5.63 (d, 1H, $J_{3',4'}$ = 10.1 Hz, $H_{3'}$), 6.12 (dd, 1H, $J_{3',4'}$ = 10.1 Hz, $J_{4',5'}$ = 3.7 Hz, $H_{4'}$), 6.90 (d, 1H, $J_{5,6}$ = 8.1 Hz, H_5), 7.06 (dd, 1H, $J_{7,8}$ = 7.7, $J_{6,7}$ = 7.7 Hz, H_7), 7.23 (dd, 1H, $J_{5,6}$ = 8.1, $J_{6,7}$ = 7.7 Hz, H_6), 7.33 (d, 1H, $J_{7,8}$ = 7.7 Hz, H_8), 8.22 (s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 21.2 (2 x CH_3), 21.4 (CH_3), 66.6 (C-6'), 68.6 (C-5'), 69.4 (C-4'), 68.6 (C-3'), 83.0 (C-2), 117.2 (C-5), 116.4 (C-8a), 124.7 (C-7), 128.0 (C-6), 128.3 (C-8), 134.4 (C-4a), 161.9 (C-3), 170.3 (CO), 170.6 (CO), 170.9 (CO); ms: m/z 409 (M^+, 33), 367 (17), 277 (19), 247 (9), 206 (8), 180 (22), 152 (19), 43 (100).

Anal. Calcd. for $C_{18}H_{19}NO_8S$: H, 4.68; N, 3.42. Found: H, 4.82; N, 3.22.

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