An Approach to *C*-Branched and Heterocyclic Anellated Pyranosides by Reaction of α-D-*erythro*-Hexopyranosid-2-ulose with Orthoformic Acid Derivatives [1])

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Dedicated to Professor Dr. Manfred Schulz on the Occasion of his 70th Birthday

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Abstract. The push-pull functionalization of the ulose **1** to give the (*E*)-configurated dimethylaminomethylene pyranosidulose **2** was achieved with bis(dimethylamino)*tert*-butoxymethane. Substitution of the dimethylamino group by different amines provided the corresponding sugar enamines **3** as (*Z*) isomers. **2** reacted with hydrazine hydrate to furnish the pyrano[3,4-*c*]pyrazole **4**. Treatment of **2** with acetamidine hydrochloride, benzamidine hydrochloride, *S*-methylisothiouronium methylsulfate and guanidine carbonate, respectively, in the presence of bases yielded the pyrimidoanellated pyranosides **5**. Reaction of **2**, ethyl 2-cyano-acetimidate hydrochloride **7** and sodium hydride afforded a mixture of a pyrido- and pyranoanellated pyranoside **9** and **10**, respectively.

C-Branched sugars have become an increasingly important area in synthetic organic chemistry, especially as constituents of antibiotics, glycosyl inhibitors and other natural products [1–6]. Several methods for the synthesis of *C*-branched sugars are known [7–11]. Recently, we have developed approaches involving the reaction of carbanions of deoxy uloses with carbon disulfide and alkyl halide in the presence of sodium hydride to give push-pull functionalized α-oxoketene dithioacetals with a sugar moiety, such as methyl 4,6-*O*-benzylidene-3-[bis(methylthio)methylene]-3-deoxy-α-D-*erythro*-hexo-pyranosid-2-ulose (**1**) and the corresponding 4,6-*O*-benzylidene-2-[bis(methylthio)methylene]-2-deoxy-3-ulose [12].

On the other hand, fused ring systems with a pyran moiety are also very interesting as potential inhibitors of glycosidases [13, 14]. Therefore, the development of new methods for the synthesis of anellated pyranose derivatives has become a topic of current interest in synthetic organic chemistry in recent years [15–18]. We describe herein the synthesis and cyclization of branched chain pyranosides with push-pull activity using orthoformic acid derivatives.

Results and Discussion

In earlier works we found that only one donor group in push-pull activated β-alkylthioenone in comparison with α-oxoketene acetals containing two push groups rises the reactivity of such systems [19]. Bredereck and coworkers reported the reaction of acidic methylene compounds with acetals of amides [20]. Similarly, compound **1** reacted with *N*,*N*-dimethylformamide dimethyl acetal and bis(dimethylamino)*tert*-butoxymethane, respectively, in tetrahydrofuran to furnish the branched chain ulose **2** in acceptable yields (Scheme 1). In a NOESY experiment of compound **2**, correlations were found only between NMe_2 and 4-H as well as C<u>H</u>Ph conforming the (*Z*) configuration.

The dimethylaminomethylene ulose **2** with push-pull functionality should serve for displacement reactions of the dimethylamino group. The higher reactivity attributed to the presence of only one donor group in this push-pull system reflects the straightforward substitution of the dimethylamino group by treatment of compound **2** with ammonia, *p*-*tert*-butylaniline, *p*-chloroaniline and *o*-phenylenediamine leading to the formation of the sugar enamines **3** in good yields. According to IR and NMR spectra the formation of an intramolecular hydrogen bond is favoured and, therefore, all products posses the (*Z*) configuration. Except compound **3b**, all other substances were got as solids.

Furthermore, the dimethylaminomethylene ulose **2** reacted with hydrazine hydrate to give the pyrano[3,4-*c*]pyrazole **4** in 80% yield. We prepared some times before this compound by reaction of methyl 4,6-*O*-benzylidene-3-[bis(methylthio)methylene]-3-deoxy-α-D-

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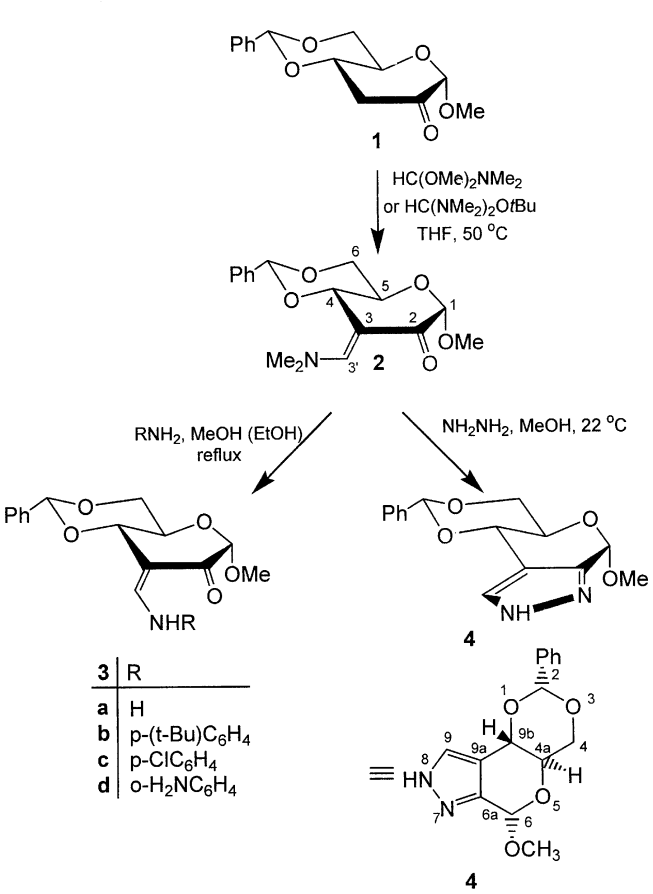
erythro-hexopyranosid-2-ulose followed by dethioalkylation and treatment with hydrazine hydrate in a lower overall yield [19].

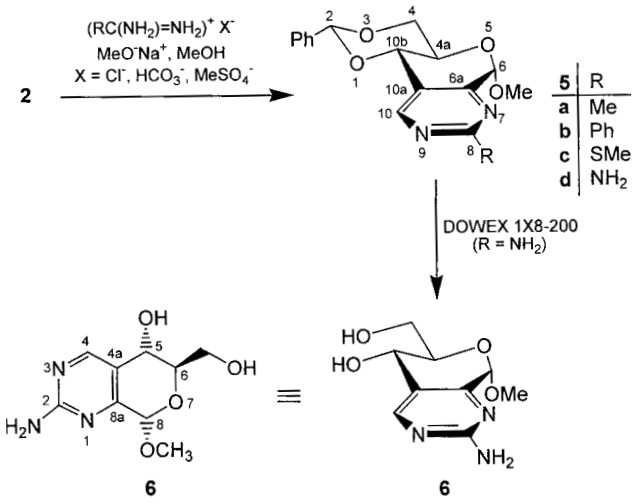


Scheme 1 Preparation of the dimethylaminomethylene pyranosidulose **2** and reactions with amines and hydrazine

Similarly, the ulose **2** was allowed to react with acetamidine hydrochloride, benzamidine hydrochloride, *S*-methylisothiouronium methylsulfate and guanidinium carbonate in methanol in the presence of sodium methanolate in order to synthesize the corresponding pyrimidoanellated pyranosides **5** isolated as crystalline compounds in yields of 60 to 70% (Scheme 2). As expected, no signals of a dimethylamino and carbonyl group in the NMR spectra could be observed. The mass spectra showed the characteristic molecule peaks.

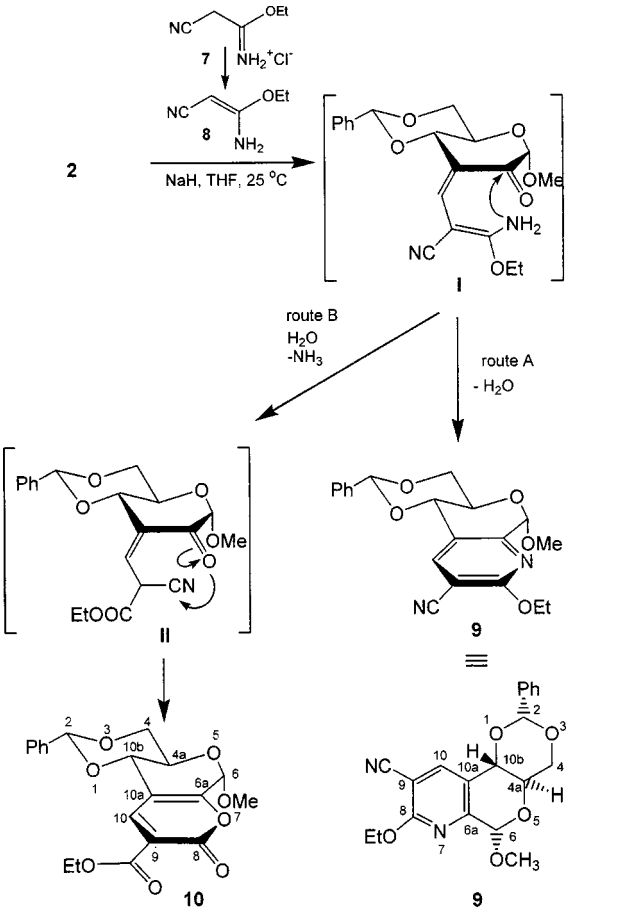
In the case of compound **5d** we tried the deprotection in a solution of **5d** in tetrahydrofuran with hydrochloric acid. The benzylidene group was completely removed and the pyrimidoanellated pyranoside **6** could be obtained in 71% yield.

Furthermore, the dimethylaminomethylene ulose **2** reacted with ethyl 2-cyano-acetimidate hydrochloride **7** [21] to furnish a mixture of the both compounds **9** and **10** in 40% and 27% yield, respectively. The pyranoanellated pyranoside **10** was also prepared by treat-



Scheme 2 Reactions of the dimethylaminomethylene pyranosidulose **2** with amidines and related compounds

ment of methyl (3*Z*)-4,6-*O*-benzylidene-3-deoxy-3-[(methylthio)methylene]-α-*D*-*erythro*-hexopyranosid-2-ulose with diethyl malonate in anhydrous *N*,*N*-dimethylformamide in the presence of potassium carbonate [22].



Scheme 3 Reactions of the dimethylaminomethylene pyranosidulose **2** with 2-cyano-acetimidate

As shown in Scheme 3 the postulated mechanism involves a substitution of the dimethylamino group by attack of the corresponding enaminonitrile **8** with the α-carbon atom to give the intermediate I. The following step is the cyclization involving the amino and carbonyl group to yield the pyridoanellated pyranoside **9** (route A). On the other hand, the hydrolysis of the intermediate enaminonitrile I could afforded the ethyl cyanoacetate II which undergoes the nitrile cyclization and hydrolysis to afford the pyranoanellated pyranoside **10**.

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Experimental

Melting points were determined with a Boëtius apparatus and are corrected. IR spectra were recorded with a Nicolet 205 FT-IR spectrometer. Specific optical rotations were measured with a Gyromat HP (Dr. Kernchen). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker instruments ARX 300 and AC 250 with $CDCl_3$ or DMSO-d_6 as solvent. The calibration of spectra was carried out by means of solvent peaks (DMSO-d_6: δ ^{1}H = 2.50; δ ^{13}C = 39.7; $CDCl_3$: δ ^{1}H = 7.25; δ ^{13}C = 77.0). The ^{13}C NMR signals were assigned by DEPT and/or ^{1}H,^{13}C COSY experiments. The mass spectra were recorded on an AMD 402/3 spectrometer AMD Intectra GmbH. For chromatography Merck silica gel 60 (63–200 µm) was used. TLC was performed on silica gel 60 GF_{254} (Merck) with detection by charring with sulfuric acid. For HPLC Nucleosil 100, 7 µm, 20 ml/min and a UV-detector (Knauer) were used. Elemental analysis were performed on a Leco CHNS-932 instrument. The solvents and liquid reagents were purified and dried according to recommended procedures.

Methyl (3E)-4,6-O-Benzylidene-3-[(dimethylamino)ethylene]-3-deoxy-α-D-erythro-hexopyranosid-2-ulose (**2**)

135 mg (0.51 mol) **1** and 100 mg (0.57 mol) bis(dimethylamino)-*tert*-butoxy-methane in 10 ml anhydrous THF were stirred at 50 °C for 3 h. After completion of the reaction (monitored by TLC; occasionally further addition of the reagent) the solvent was evaporated *in vacuo* and the residue purified by column chromatography [$CHCl_3$/ethyl acetate (3:1)]. Crystallization from ethanol afforded 130 mg (79%) of **2**, *m.p.* 199 °C (ethanol); $[\alpha]_D^{19}$ = +217 (c = 1.0, $CHCl_3$); R_f = 0.21 (ethyl acetate). – IR (KBr): ν/cm^{-1} = 1558 (C=C), 1662 (C=O). – ^{1}H NMR (250 MHz, $CDCl_3$): δ/ppm = 3.06 (s, 6H, Me_2N), 3.48 (s, 3H, MeO), 3.86 (dd, 1H, $J_{5,6a}$ = 10.4 Hz, $J_{6a.6e}$ = 10.1 Hz, 6a-H), 4.12 (ddd, 1H, 5-H), 4.49 (dd, 1H, $J_{5,6e}$ = 4.6 Hz, 6e-H), 4.62 (s, 1H, 1-H), 4.69 (d, 1H, $J_{4,5}$ = 9.0 Hz, 4-H), 5.61 (s, 1H, C<u>H</u>Ph), 7.31–7.49 (m, 5H, Ph), 7.71 (s, 1H, 3'-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$): δ/ppm = 40.2, 47.3 (2 × br, Me_2N), 56.1 (MeO), 65.5 (C-5), 69.4 (C-6), 76.7 (C-4), 100.1 (C-1), 100.4 (C-3), 101.1 (<u>C</u>HPh), 126.3 (*o*-Ph), 128.4 (*m*-Ph), 129.2 (*p*-Ph), 137.6 (*i*-Ph), 154.4 (C-3'), 188.0 (C-2). – MS : *m/z* = 320 $[M+H]^+$.

$C_{17}H_{21}NO_5$	Calcd.: C 63.93	H 6.62	N 4.38
(319.35)	Found: C 63.89	H 6.65	N 4.53.

Methyl 3(Z)-(Aminomethylene)-4,6-O-benzylidene-3-deoxy-α-D-erythro-hexopyranosid-2-ulose (**3a**)

160 mg (0.60 mmol) of **2** and 10 ml of a saturated solution of ammonia in 10 ml anhydrous methanol were stirred until the completion of the reaction was achieved (1–3 h, monitored by TLC). The precipitate was filtered, the solvent was evaporated, and the collected solids were recrystallized from ethanol. Yield 131 mg (75%), white needles; *m.p.* 229–230 °C (ethanol) [19].

Preparation of Sugar Enamines 3b–d (General Procedure)

160 mg (0.60 mmol) of **2** and 0.60 mmol of the corresponding amine in 10 ml anhydrous ethanol were heated under reflux until the completion of the reaction was achieved (1–3 h, monitored by TLC). The solvent was evaporated, and the solid (except compound **3b**) was recrystallized from ethanol.

Methyl 4,6-O-Benzylidene-3(Z)-(p-tert-butyl-anilinomethylene)-3-deoxy-α-D-erythro-hexopyranosid-2-ulose (**3b**)

From **2** and *p-tert*-butylaniline. Yield 192 mg (75%), yellow wax; $[\alpha]_D^{23}$ = –219 (*c* = 1.0, $CHCl_3$); R_f = 0.30 ($CHCl_3$). – IR (KBr): ν/cm^{-1} = 1567 (C=C), 1652 (C=O), 2961 (N–H). – ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 1.30 (s, 9H, Me_3C), 3.57 (s, 3H, MeO), 3.87 (dd, 1H, $J_{5,6a}$ = 10.0 Hz, $J_{6a.6e}$ = 10.2 Hz, 6a-H), 4.10 (ddd, 1H, 5-H), 4.37 (dd, 1H, $J_{5,6e}$ = 4.8 Hz, 6e-H), 4.57 (dd, 1H, $J_{4,5}$ = 9.5 Hz, $J_{4,3'}$ = 1.1 Hz, 4-H), 4.74 (s, 1H, 1-H), 5.69 (s, 1H, C<u>H</u>Ph), 7.00 (m, 2H, C_6H_4), 7.33 (m, 2H, C_6H_4), 7.37–7.59 (m, 5H, Ph), 7.69 (dd, 1H, $J_{3',NH}$ = 13.0 Hz, 3'-H), 12.00 (br d, 1H, NH). – ^{13}C NMR (75.5 MHz, $CDCl_3$): δ/ppm = 31.2 (Me), 34.3 ($Me_3\underline{C}$), 56.3 (MeO), 64.6 (C-5), 69.1 (C-6), 75.8 (C-4), 99.2 (C-1), 101.2 (CHPh), 102.8 (C-3), 116.8 (*o*-C_6H_4NH), 126.3 (*o*-Ph), 126.5 (*m*-C_6H_4NH), 128.2 (*m*-Ph), 129.1 (*p*-Ph), 136.9 (*p*-C_6H_4NH), 137.4 (*i*-Ph), 144.4 (C-3'), 147.7 (*i*-C_6H_4NH), 188.6 (C-2). – MS : *m/z* = 423.0 $[M+H]^+$.

$C_{25}H_{29}NO_5$	Calcd.: C 70.90	H 6.90	N 3.30
(423.50)	Found: C 71.49	H 6.70	N 3.19.

Methyl 4,6-O-Benzylidene-3(Z)-(p-chloro-anilinomethylene)-3-deoxy-α-D-erythro-hexopyranosid-2-ulose (**3c**)

From **2** and *p*-chloroaniline. Yield 192 mg (79%), yellow-greenish needles; *m.p.* 205–208 °C (ethanol); $[\alpha]_D^{21}$ = –244 (*c* = 1.0, $CHCl_3$); R_f = 0.27 ($CHCl_3$). – IR (KBr): ν/cm^{-1} = 1569 (C=C), 1659 (C=O), 3257 (N–H). – ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 3.54 (s, 3H, MeO), 3.85 (dd, 1H, $J_{5,6a}$ = 10.0 Hz, $J_{6a.6e}$ = 10.2 Hz, 6a-H), 4.07 (ddd, 1H, 5-H), 4.36 (dd, 1H, $J_{5,6e}$ = 4.8 Hz, 6e-H), 4.54 (dd, 1H, $J_{4,5}$ = 9.5 Hz, $J_{4,3'}$ = 1.0 Hz, 4-H), 4.72 (s, 1H, 1-H), 5.67 (s, 1H, C<u>H</u>Ph), 6.98 (m, 2H, C_6H_4), 7.27 (m, 2H, C_6H_4), 7.37–7.55 (m, 5H, Ph), 7.57 (dd, 1H, $J_{3',NH}$ = 13.0 Hz, 3'-H), 12.01 (br d, 1H, NH). – ^{13}C NMR (75.5 MHz, $CDCl_3$): δ/ppm = 56.4 (MeO), 64.6 (C-5), 69.1 (C-6), 75.8 (C-4), 99.2 (C-1), 101.5 (<u>C</u>HPh), 103.9 (C-3), 118.1 (*o*-C_6H_4NH), 126.4 (*o*-Ph), 128.4 (*m*-Ph), 129.3 (*p*-Ph), 129.8 (*m*-C_6H_4NH), 137.3 (*i*-Ph), 138.1 (*i*-C_6H_4NH), 143.5 (C-3'), 189.5 (C-2). – MS: *m/z* = 400.9 $[M]^+$.

$C_{21}H_{19}ClNO_5$	Calcd.: C 62.92	H 4.77	N 3.49
(400.83)	Found: C 62.42	H 5.01	N 3.53.

Methyl 3(Z)-(o-Amino-anilinomethylene)-4,6-O-benzylidene-3-deoxy-α-D-erythro-hexopyranosid-2-ulose (**3d**)

From **2** and *o*-phenylenediamine. Yield 183 mg (79%), yellow prisms; *m.p.* 196 °C (ethanol); $[\alpha]_D^{23} = -160$ (*c* = 1.0, $CHCl_3$); R_f = 0.34 [$CHCl_3$/ethyl acetate (3:1)]. – IR (KBr): ν/cm^{-1} = 1562 (C=C), 1649 (C=O), 2971 (N–H), 3222, 3366 (NH_2). – ^{1}H NMR (250 MHz, $CDCl_3$): δ/ppm = 3.55 (s, 3H, MeO), 3.69 (br, 2H, NH_2), 3.86 (dd, 1H, $J_{5,6a} = J_{6a.6e}$ = 10.0 Hz, 6a-H), 4.08 (ddd, 1H, 5-H), 4.36 (dd, 1H, $J_{5,6e}$ = 4.9 Hz, 6e-H), 4.56 (dd, 1H, $J_{4,5}$ = 9.2 Hz, $J_{4,3'}$ = 1.0 Hz, 4-H), 4.75 (s, 1H, 1-H), 5.68 (s, 1H, CHPh), 6.77 (m, 2H, C_6H_4), 7.01 (m, 2H, C_6H_4), 7.36–7.54 (m, 5H, Ph), 7.62 (dd, 1H, $J_{3',NH}$ = 13.0 Hz, 3'-H), 12.05 (br d, 1H, NH). – ^{13}C NMR (100.6 MHz, $CDCl_3$): δ/ppm = 56.5 (MeO), 64.8 (C-5), 69.2 (C-6), 75.8 (C-4), 99.3 (C-1), 101.4 (CHPh), 102.7 (C-3), 117.3, 118.6, 119.9 (C_6H_4), 126.4 (*o*-Ph), 128.4 (*m*-Ph), 129.2 (*p*-Ph), 137.3 (*i*-Ph), 146.6 (C-3'), 188.6 (C-2). – MS : *m/z* = 383 $[M+H]^+$.

$C_{21}H_{22}N_2O_5$	Calcd.: C 65.96	H 5.80	N 7.32
(382.41)	Found: C 66.05	H 5.74	N 7.22.

[2R-(2α,4aα,6α,9bβ))-4,4a,6,9b-Tetrahydro-2-phenyl-7H-1,3-dioxino[4',5':5,6]-pyrano[3,4-c]pyrazol-6-yl methylether (**4**)

To a stirred anhydrous methanolic solution of 100 mg (0.31 mmol) **2**, 0.05 ml (1.02 mmol) hydrazine hydrate were added. After 20 min the mixture was evaporated to dryness. Recrystallization from a small amount of ethanol (storage at –40 °C for 3 days) afforded 72 mg (80%) of **4**; *m.p.* 220 °C decomp.[19].

Preparation of Pyrimidoanellated Pyranosides 5 (General Procedure)

A mixture of 160 mg (0.50 mmol) **2**, 1.00 mmol acetamidine and benzamidine hydrochloride, respectively, or 0.50 mmol *S*-methylthiouronium sulfate and guanidine carbonate, respectively, 162 mg (3 mmol) sodium methanolate and 20 ml dry methanol was refluxed. After the reaction had completed (t.l.c. control) the mixture was cooled down to 20 °C, treated with 80 ml of a saturated solution of ammonium chloride in water. The methanol was removed *in vacuo* und the water solution three times extracted with dichloromethane. After concentration the residue was purified by column chromatography [toluene/ethyl acetate (10:1)]. Crystallization from ethanol (methanol) afforded the pure compounds.

[2R-(2α,4aα,6α,10bβ)]-4,4a,6,10b-Tetrahydro-8-methyl-2-phenyl-1,3-dioxino[4',5':5,6]pyrano[3,4-d]pyrimidin-6-yl methyl ether (**5a**)

From **2** and acetamidine hydrochloride. Reaction time 2.5 h. Yield 110 mg (70%), colourless needles; *m.p.* 186–188 °C (ethanol) $[\alpha]_D^{23}$ = 45.3 (*c* = 1.0, $CHCl_3$); R_f = 0.29 (toluene/ethyl acetate = 10:1). – ^{1}H NMR (250 MHz, $CDCl_3$): δ/ppm = 2.77 (s, 3H, Me), 3.64 (s, 3H, MeO), 3.95 (dd, 1H, $J_{4\alpha,4\beta}$ = 10.2 Hz, $J_{4\beta,4a}$ = 10.0, 4β-H), 4.15 (ddd, 1H, 4a-H), 4.43 (dd, 1H, $J_{4\alpha,4a}$ = 4.9 Hz, 4α-H), 4.74 (dd, 1H, $J_{10,10b}$ = 0.8, $J_{4a,10b}$ = 9.5 Hz, 10b-H), 5.39 (s, 1H, 6-H), 5.75 (s, 1H, 2-H), 7.38–7.55 (m, 5H, Ph), 8.77 (d, 1H, 10-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$): δ/ppm = 26.0 (Me), 56.7 (MeO), 63.2 (C-4a), 69.3 (C-4), 74.1 (C-10b), 97.8 (C-6), 102.1 (C-2), 124.7 (C-10a), 126.3 (*o*-Ph), 128.4 (*m*-Ph), 129.4 (*p*-Ph), 136.8 (*i*-Ph), 154.0 (C-10), 159.4 (C-6a), 168.0 (C-8). – MS (CI-isobutane) : *m/z* (%) = 315.1 (100) $[M+H]^+$.

$C_{17}H_{18}N_2O_4$	Calcd.: N 8.91		
(314.33)	Found: N 8.30.		

[2R-(2α,4aα,6α,10bβ)]-4,4a,6,10b-Tetrahydro-6-methoxy-2,8-diphenyl-1,3-dioxino[4',5':5,6]pyrano[3,4-d]pyrimidin-2-yl methyl ether (**5b**)

From **2** and benzamidine hydrochloride. Reaction time 4 h. Yield 130 mg (69%), colourless needles; *m.p.* 200–201 °C (ethanol) $[\alpha]_D^{23}$ = 46.4 (*c* = 1.0, $CHCl_3$); R_f = 0.27 (toluene/ethyl acetate = 10:1). – ^{1}H NMR (250 MHz, $CDCl_3$): δ/ppm = 3.68 (s, 3H, MeO), 3.98 (dd, 1H, $J_{4\alpha,4\beta}$ = 10.2 Hz, $J_{4\beta,4a}$ = 10.0, 4β-H), 4.23 (ddd, 1H, 4a-H), 4.46 (dd, 1H, $J_{4\alpha,4a}$ = 4.9 Hz, 4α-H), 4.80 (dd, 1H, $J_{4a,10b}$ = 9.5 Hz, 10b-H), 5.47 (s, 1H, 6-H), 5.78 (s, 1H, 2-H), 7.39–7.57 (m, 8H, 2-Ph, 8-Ph), 8.44 (m, 2H, 8-*o*-Ph), 8.93 (d, $J_{10,10b}$ = 0.8 Hz, 10-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$): δ/ppm = 56.7 (MeO), 63.3 (C-4a), 69.4 (C-4), 74.3 (C-10b), 98.2 (C-6), 102.1 (C-2), 125.4 (C-10a), 126.3 (2-*o*-Ph), 128.4 (2-*m*-Ph), 128.5 (8-*o*-, 8-*m*-Ph), 129.4 (2-*p*-Ph), 130.8 (8-*p*-Ph), 136.9 (2-*i*-Ph), 137.1 (8-*i*-Ph), 154.2 (C-10), 159.8 (C-6a), 164.5 (C-8). – MS (CI-isobutane): *m/z* (%) = 377 (100) $[M+H]^+$

$C_{22}H_{20}N_2O_4$	Calcd.: C 70.20	H 5.35	N 7.44
(388.37)	Found: C 70.16	H 5.37	N 7.49.

[2R-(2α,4aα,6α,10bβ)]-4,4a,6,10b-Tetrahydro-6-methoxy-8-methylthio-2-phenyl-1,3-dioxino[4',5':5,6]pyrano[3,4-d] pyrimidin-2-yl methyl ether (**5c**)

From **2** and *S*-methylisothiouronium sulfate. Reaction time 8 h. Yield 102 mg (59%), colourless needles; *m.p.* 180 °C decomp.(ethanol) $[\alpha]_D^{23}$ = 43.1 (*c* = 1.0, $CHCl_3$); R_f = 0.24 (toluene/ethyl acetate = 10:1). – ^{1}H NMR (250 MHz, $CDCl_3$): δ/ppm = 2.56 (s, 3H, MeS), 3.61 (s, 3H, MeO), 3.94 (dd, 1H, $J_{4\alpha,4\beta}$ = 10.1 Hz, $J_{4\beta,4a}$ = 10.0, , 4β-H), 4.14 (ddd, 1H, 4a-H), 4.42 (dd, 1H, $J_{4\alpha,4a}$ = 4.9 Hz, 4α-H), 4.51 (dd, 1H, $J_{4a,10b}$ = 9.5 Hz, $J_{10,10b}$ = 0.8 Hz, 10b-H), 5.33 (s, 1H, 6-H), 5.74 (s, 1H, 2-H), 7.38–7.54 (m, 5H, Ph), 8.65 (d, 1H, 10-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$): δ/ppm = 14.2 (MeS), 56.7 (MeO), 63.4 (C-4a), 69.3 (C-4), 74.1 (C-10b), 97.9 (C-6), 102.1 (C-2), 122.7 (C-10a), 126.3 (*o*-Ph), 128.3 (*m*-Ph), 129.3 (*p*-Ph), 137.0 (*i*-Ph), 154.1 (C-10), 159.8 (C-6a), 172.6 (C-8). – MS (70 eV): *m/z* (%) = 345.9 (10) $[M]^+$, 316.1 (100).

$C_{17}H_{18}N_2O_4S$	Calcd.: C 58.94	H 5.24	N 8.09	S 9.26
(388.37)	Found: C 58.82	H 5.35	N 8.22	S 9.32.

[2R-(2α,4aα,6α,10bβ)]-8-Amino-4,4a,6,10b-tetrahydro-6-methoxy-2-phenyl-1,3-dioxino[4',5':5,6]pyrano[3,4-d]pyrimidin-2-yl methyl ether hydrate (**5d**)

From **2** and guanidine carbonate. Reaction time 1.5 h. Yield 120 mg (72%), colourless needles; *m.p.* 233–235 °C (methanol) $[\alpha]_D^{23}$ = 40.1 (*c* = 1.0, $CHCl_3$); R_f = 0.31 ($CHCl_3$/ethyl acetate). – IR (Nujol): ν/cm^{-1} = 3198, 3308 (NH_2). – ^{1}H NMR (250 MHz, $CDCl_3$): δ/ppm = 3.60 (s, 3H, MeO), 3.92 (dd, 1H, $J_{4\beta,4a} = J_{4\alpha,4\beta}$ = 10.1 Hz, 4β-H), 4.09 (ddd, 1H, 4a-H), 4.40 (dd, 1H, $J_{4\alpha,4a}$ = 4.9 Hz, 4α-H), 4.64 (dd, 1H, $J_{4a,10b}$ = 9.5 Hz, $J_{10,10b}$ = 0.9 Hz, 10b-H), 5.22 (s, 1H, 6-H), 5.29 (s, 2H, NH_2), 5.72 (s, 1H, 2-H), 7.36–7.55 (m, 5H, Ph), 8.43 (d, 1H, 10-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$): δ/ppm = 56.4 (MeO), 63.9 (C-4a), 69.2 (C-4), 74.2 (C-10b), 97.9 (C-6), 101.8 (C-2), 117.9 (C-10a), 126.3 (*o*-Ph), 128.3 (*m*-Ph), 129.3 (*p*-Ph), 137.1 (*i*-Ph), 155.7 (C-10), 160.6 (C-6a), 162.7

(C-8). – MS (70 eV): *m/z* (%) = 315.2 (8) $[M–H_2O]^+$, 166.1 (100).

$C_{16}H_{17}N_3O_4 \cdot H_2O$ (388.37) Calcd.: N 12.60 Found: N 12.15.

[5S-(5α,6β,8α)]-2-Amino-5,8-dihydro-6-hydroxymethyl-8-methoxy-pyrano[3,4-d]-pyrimidin-5-ol (**6**)

A solution of 180 mg (0.54 mmol) **5d**, 2 ml 1N HCl and 15 ml tetrahydrofuran was allowed to stand at 25 °C for 20 h. The solution was consecutively passed through a anion-exchange column (DOWEX, 1X8-200; OH^-), concentrated to a syrup and purified by column chromatography (ethanol/ethyl acetate = 1:1). Yield 87 mg (71%), colourless needles; *m.p.* 180 °C decomp.(ethanol/water); $[\alpha]_D^{23} = 20.4$ ($c = 0.2$, H_2O); $R_f = 0.61$ (ethanol/ethyl acetate = 1:1). – ^{1}H NMR (300 MHz, D_2O): δ/ppm = 3.77 (s, 3H, MeO), 4.07 (m, 1H, CH_2,), 4.19 (d, 1H, 5-H), 4.83 (m, 1H, 6-H), 5.47 (s, 1H, 8-H), 5.72 (s, 1H, 2-H), 7.30 (br, 2H, OH, NH_2), 8.69 (s, 1H, 10-H). – ^{13}C NMR (75.5 MHz, D_2O): δ/ppm = 56.5 (MeO), 61.1 (CH_2), 62.5 (C-6), 73.0 (C-5), 97.1 (C-8), 120.6 (C-4a), 159.4 (C-4), 160.6 (C-8a), 162.2 (C-2). – MS (70 eV): *m/z* (%) = 227.0 (9) $[M]^+$, 151.2 (100).

[2R-(2α,4aα,6α,10bβ)]-8-Ethoxy-4,4a,6,10b-tetrahydro-6-methoxy-2-phenyl-1,3-dioxino[4',5':5,6]pyrano[3,4-b]pyridine-9-carbonitril (**9**) and *[2R-(2α,4aα,6β,10bβ-Tetrahydro-6α-methoxy-8-oxo-2α-phenyl-pyrano[3',2':4,5]pyrano[3,2-d][1,3]dioxin-9-carbonsäure-ethylester* (**10**)

To a solution of 118 mg (0.37 mmol) **2** in 15 ml tetrahydrofuran 55 mg (0.37 mmol) ethyl 2-cyano-acetimidate hydrochloride (**7**) [21] and 60 mg (1.50 mmol) sodium hydride (60% in mineral oil) were added at 0 °C under stirring. The mixture was warmed within 3 h to 20 °C. A saturated aqueous solution of NH_4Cl was added to adjust the pH to near 6. The tetrahydrofuran was evaporated *in vacuo* and the residue was extracted three times with 15 ml dichloromethane. The combined organic layer was dried over Na_2SO_4. The solvent was distilled off and the residual mixture was separated by means of silicagel (eluent: toluene).

9: Yield 54 mg (40%), colourless needles; *m.p.* 196–198 °C (methanol) $[\alpha]_D^{23} = -40.1$ (c = 1.0, $CHCl_3$). – IR (Nujol): ν/cm^{-1} = 2225 (CN). – ^{1}H NMR (250 MHz, $CDCl_3$): δ/ppm = 1.43 (t, 3H, $J_{CH3,CH2}$ = 7.0 Hz, $CH_2C\underline{H}_3$), 3.61 (s, 3H, MeO), 3.92 (dd, 1H, $J_{4\beta,4a} = J_{4\alpha,4\beta}$ = 10.1 Hz, 4β-H), 4.14 (ddd, 1H, 4a-H), 4.42 (dd, 1H, $J_{4\alpha,4a}$ = 4.8 Hz, 4α-H), 4.50 (m, 2H, $C\underline{H}_2CH_3$), 4.63 (dd, 1H, $J_{4a,10b}$ = 9.8 Hz, 10b-H), 5.32 (s, 1H, 6-H), 5.72 (s, 1H, 2-H), 7.35–7.57 (m, 5H, Ph), 7.99 (d, 1H, $J_{10,10b}$ = 0.9 Hz, 10-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$): δ/ppm = 14.2 ($CH_2\underline{C}H_3$), 56.6 (MeO), 63.4 (C-4a), 63.7 ($\underline{C}H_2CH_3$), 69.2 (C-4), 74.7 (C-10b), 97.2 (C-9), 98.3 (C-6), 102.1 (C-2), 114.8 (CN), 123.5 (C-10a), 126.2 (*o*-Ph), 128.4 (*m*-Ph), 129.4 (*p*-Ph), 136.9 (*i*-Ph), 139.6 (C-10), 153.5 (C-6a), 163.2 (C-8). – MS (70 eV): *m/z* (%) = 368.2 (10) $[M]^+$, 219.1 (100).

$C_{20}H_{20}N_2O_5$ (388.37) Calcd.: C 65.20 H 5.47 N 7.60 Found: C 65.03 H 5.34 N 7.45.

10: Yield 54 mg (27%), colourless needles; *m.p.* 150–152 °C (ethanol) $[\alpha]_D^{23} = -16.5$ (c = 1.0, $CHCl_3$). – ^{1}H NMR (250 MHz, $CDCl_3$): δ/ppm = 1.33 (t, 3H, $J_{CH3,CH2}$ = 7.0 Hz, $CH_2C\underline{H}_3$), 3.57 (s, 1H, OMe), 3.89 (dd, 1H, $J_{4\beta,4\alpha}$ = 10.1 Hz, $J_{4\alpha,4\beta}$ = 10.2 Hz, H-4β), 4.09 (ddd, 1H, $J_{4a,10b}$ = 9.5 Hz, $J_{4a,4\alpha}$ = 4.8 Hz, H-4a), 4.25–4.38 (m, 3H, H-4α/$C\underline{H}_2CH_3$), 4.49 (d, 1H, H-10b), 5.12 (s, 1H, H-6), 5.66 (s, 1H, H-2), 7.38–7.52 (m, 5H, Ph), 8.21 (s, 1H, H-10). – ^{13}C NMR (62.9 MHz, $CDCl_3$): δ/ppm = 14.2 ($CH_2\underline{C}H_3$), 57.0 (OMe), 62.0 ($\underline{C}H_2CH_3$), 64.5 (C-4a), 68.8 (C-4), 73.4 (C-10b), 94.9 (C-6), 102.3 (C-2), 113.6 (C-10a), 118.2 (C-9), 126.3 (*o*-Ph), 128.4 (*m*-Ph), 129.5 (*p*-Ph), 136.7 (*i*-Ph), 144.8 (C-10), 156.2, 157.7 (C-6a, C-8), 162.7 (*C*OOEt). – MS (CI-isobutane): *m/z* (%) = 389 (100) $[M+H]^+$.

$C_{20}H_{20}O_8$ (388.37) Calcd.: C 61.85 H 5.19 Found: C 61.85 H 5.08.

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