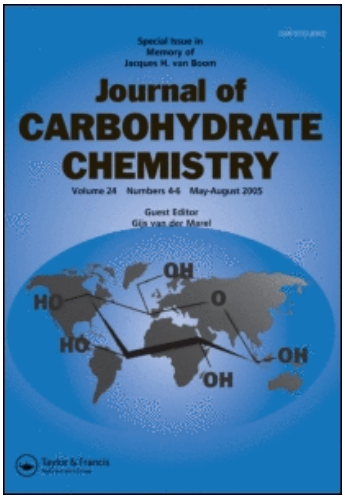

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Synthesis of Pyrano- and Pyrido-Anellated Pyranosides as Precursors for Nucleoside Analogues

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The push-pull activated methyl (3*Z*)-4,6-*O*-benzylidene-3-[(methylthio)methylene]-3-deoxy-α-D-*erythro*-hexopyranosid-2-ulose (**1**) reacted with dialkyl malonate in the presence of potassium carbonate to give the alkyl (2*R*,4a*R*,6*S*,10b*S*)-4a,6,8,10b-tetrahydro-6-methoxy-8-oxo-2-phenyl-4*H*-pyrano[3′,2′:4,5]pyrano[3,2-*d*][1,3]dioxine-9-carboxylates **2** and **3**. Treatment of **1** with 3-oxo-*N*-phenyl-butyramide, *N*-(4-methoxy-phenyl)-3-oxo-butyramide, and 3-oxo-*N*-*o*-tolyl-butyramide, respectively, in the presence of potassium carbonate and 18-crown-6 yielded the (2*R*,4a*R*,6*S*,10b*S*)-9-acetyl-7-aryl-4,4a,7,10b-tetrahydro-6-methoxy-2-phenyl[1,3]dioxino-[4′,5′:5,6]pyrano[3,4-*b*]pyridin-8 (6*H*)-ones **4**–**6**. (2*R*,4a*R*,6*S*,10b*S*)-4,4a,8,10b-Tetrahydro-6-methoxy-8-oxo-2-phenyl-4*H*-pyrano[3′,2′:4,5]pyrano[3,2-*d*][1,3]dioxine-9-carboxamide (**7**) was prepared by anellation reactions of **1** either with malononitrile or with cyanoacetamide.

Keywords Deoxyuloses, Push-pull alkenes, Anellation, Heterocyclic fused monosaccharides

INTRODUCTION

Pyranoses and furanoses anellated with different types of heterocycles represent an interesting class of hybrid natural products. The growing

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interest on these nucleoside analogues is a result of the marked biological activities shown by numerous representatives. So, the bandwidth of these activities comprise enzyme inhibitory,[1–3] anticancer,[4–6] antibiotic,[7] and herbicidal[8] properties. Furthermore, HIV protease inhibitory effects were found[9] and such compounds could be identified as the active motif of traditional folk medicine.[10,11]

To synthesize new types of similar nucleoside analogues with potential biological activities, methods for the anellation of monosaccharides are required. Recently, we developed a new approach for the synthesis of heterocyclic fused monosaccharides. α-Deoxy uloses can easily be converted into branched-chain *push-pull* activated α-oxoketene-dithioacetals,[12,13] β-alkylthio-enones,[14,15] and β-dimethylamino-enones.[13,16] All these branched-chain uloses are suitable precursors for cyclization reactions with various nucleophiles leading to different types of heterocyclic and carbocyclic anellated monosaccharides.[12–17]

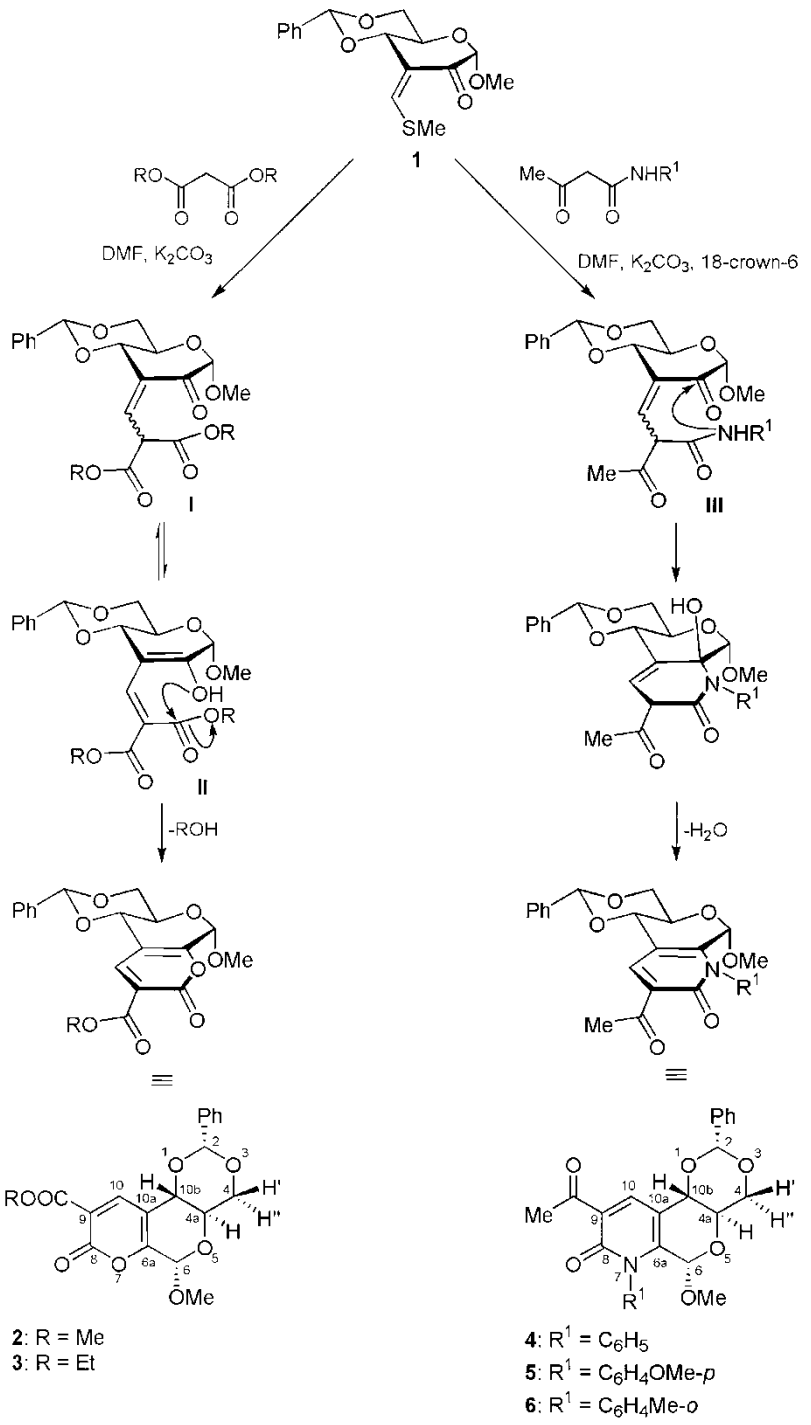
In continuing of our efforts in this field herein we want to describe the syntheses of α-pyrano- and pyrido-anellated pyranosides starting from the 3(*Z*)-3-deoxy-[(methylthio)methylene]-2-ulose **1** prepared by hydrodesulfurization of the corresponding α-oxoketene dithioacetals with tributyltin hydride or $NaBH_4$.[14]

RESULTS AND DISCUSSION

The β-methylthio-enone **1** represents a *push-pull* alkene system allowing the nucleophilic substitution of the methylthio group and a simultaneous nucleophilic attack at the carbonyl group. According to earlier examinations[14,15] in β-alkylthio-enones, displacement of the alkylthio group takes place considerably easier than in the parent α-oxoketene dithioacetals.

Treatment of **1** with diethyl malonate or dimethyl malonate using potassium carbonate as base at room temperature provided the crystalline alkyl (2*R*,4a*R*,6*S*,10b*S*)-4a,6,8,10b-tetrahydro-6-methoxy-8-oxo-2-phenyl-4*H*-pyrano[3′,2′:4,5]pyrano[3,2-*d*][1,3]dioxine-9-carboxylates **2** and **3** in 33% and 43% yield, respectively (Sch. 1). Addition of 18-crown-6 to accelerate the reaction turned out to have no effect on raising the yields, but increased amounts of decomposition products were observed. The structures of the pyrano-anellated glycosides **2** and **3** were proved by mass spectra, elemental analysis, and NMR data. In the ^{1}H and ^{13}C NMR spectra, the methylthio group, and in the ^{13}C NMR spectrum, the keto group of **1** were missing. New signals could be detected in the ^{13}C NMR spectrum for the ester carbonyl group ($\delta = 163.2$ and 162.7, respectively) and the lactone carbon atom ($\delta = 157.9$ and 157.7, respectively).

The reaction course consists of a displacement of the methylthio group by the alkyl malonate carbanion to afford the intermediate **I** and cyclization



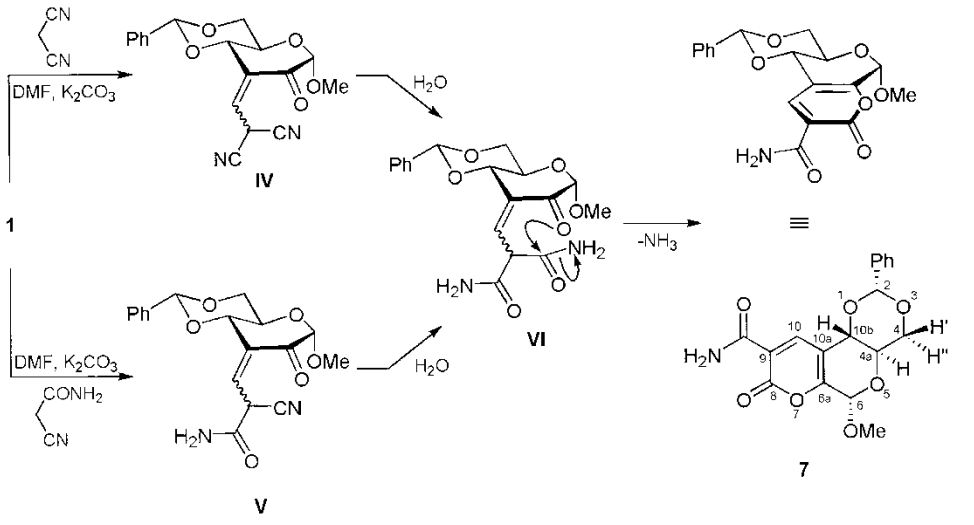
Scheme 1: Syntheses of pyrano- and pyrido-anellated pyranosides.

through substitution of an ester alkoxy group with the hydroxyl group in **II** formed in an enolization equilibrium.

Furthermore, heteroanellation reactions of β-alkylthio-enone **1** with several *N*-aryl substituted acetoacetamides were investigated. In agreement with their polyfunctionality after initial methylthio group substitution, different cyclization products are possible. In contrast to the reaction of **1** with malonates, cyclization of intermediate **III** now proceeded by reaction of the ulose carbonyl group with the arylamino function to afford the pyrido-anellated pyranosides **3**–**5** in accordance with spectroscopic data (Sch. 1). In all cases, addition of 18-crown-6 gave better results. In the ^{1}H and ^{13}C NMR spectra, the expected signals for the acetyl and the *N*-aryl group were found.

Finally, the monosaccharidic thioenolether **1** was subjected to treatment with malononitrile and cyanoacetamide. These reactions occurred comparatively fast without addition of crown ether, which caused decomposition of the reaction mixture. Surprisingly, both reagents provided only the (2*R*,4a*R*,6*S*,10b*S*)-4a,6,8,10b-tetrahydro-6-methoxy-8-oxo-2-phenyl-4*H*-pyrano-[3′,2′:4,5]pyrano[3,2-*d*][1,3]dioxine-9-carboxamide (**7**) (Sch. 2). For the preparation of pyranone **7**, the reaction of **1** with cyanoacetamide should be preferred since a purification by column chromatography is not required and the yield is higher.

The data of the elemental analysis confirmed the existence of only one nitrogen atom in the isolated compound. According to the ^{13}C NMR spectra, no nitrile group was present. In the ^{1}H NMR spectrum, two NH signals were found. One was significantly downfield ($\delta = 8.35$) caused by an intramolecular hydrogen bond to the carbonyl oxygen. The other one appeared at $\delta = 5.98$.



Scheme 2: Syntheses of pyrano-anellated pyranoside.

Furthermore, the strong similarities of the ^{13}C chemical shifts with that of compounds **2** and **3** conclusively proved structure **7**.

This outcome was in contrast to the known literature. Reactions of α-oxoketene dithioacetales with cyanoacetamide always yielded α-pyridone and not α-pyranone derivatives.[18,19] Formation of **7** can be explained as follows. First the substitution of the methylthio group of ulose **1** with malononitrile and cyanoacetamide, respectively, could yield the corresponding branched-chain sugars **IV** and **V**. As shown by TLC during aqueous workup, in both cases hydrolysis of the nitrile groups spontaneously occurred to furnish the same dicarboxamide **VI**, which underwent ring closure reaction by substitution of the amino group. Product **7** could be isolated only with two molecules of crystal water, as identified by ^1H NMR data, as well as by elemental analysis. Crystallization occurred from an ethanolic solution. Removal of the enclosed water failed, even under high vacuum conditions.

In summary, we have described routes for the synthesis of pyrano- and pyrido-anellated pyranosides. The deprotection of these compounds for biological testing is in preparation.

EXPERIMENTAL

General Methods

TLC was carried out on silica gel 60 GF_{254} (Merck) with detection by UV light ($\lambda = 254$ nm) and/or by charring with 10% sulfuric acid in methanol. Silica gel 60 (0,063–0,200 mm, Merck) was used for column chromatography with the solvent systems specified. Melting points were determined by using a Boetius melting point apparatus and are corrected. Specific rotations were determined with a Polar LμP (IBZ Messtechnik). ^1H NMR (250.13 MHz) and ^{13}C NMR (62.9 MHz) spectra were recorded on Bruker instruments AC 250 with $CDCl_3$ as solvent. The calibration of spectra was carried out on TMS (internal, ^1H) and $CDCl_3$ (^{13}C) signals (δ ^1H TMS = 0; ^{13}C $CDCl_3$ = 77.0). The ^1H and ^{13}C NMR signals were assigned by DEPT, two-dimensional ^1H, ^{13}C correlation, and/or gated decoupling experiments. The mass spectra were recorded on an AMD 402/3 spectrometer (AMD Intectra GmbH). Elemental analysis were performed on a Leco CHNS-932 instrument. The solvents and liquid reagents were purified and dried according to recommended procedures.

Methyl (2*R*,4a*R*,6*S*,10b*S*)-4a,6,8,10b-tetrahydro-6-methoxy-8-oxo-2-phenyl-4*H*-pyrano[3′,2′:4,5]pyrano[3,2-*d*][1,3]dioxine-9-carboxylate (2). Dimethyl malonate (0.225 g, 1.7 mmol) and K_2CO_3 (0.150 g, 1.1 mmol) were added to a solution of **1** (0.322 g, 1.0 mmol) in anhydrous DMF (20 mL). The mixture was stirred at rt for 5 to 6 d, until the starting material had been

consumed, as indicated by TLC. After 3 d a further small amount of K_2CO_3 was added. Then the reaction mixture was treated with a saturated aqueous $NaHSO_4$ solution (30 mL) for 20 min with stirring. After extraction with $CHCl_3$ (3 × 30 mL), the combined organic layers were washed with water (2 × 50 mL), dried (Na_2SO_4), and evaporated. Removing DMF traces was achieved by coevaporation with toluene (3 × 30 mL). Finally, the main product with R_f 0.52 (toluene-ethyl acetate 2:1) was isolated by column chromatography using the same eluent. Recrystallization from ethanol afforded **2** (125 mg, 33%) as white needles; m.p. 100–103°C; $[\alpha]_D^{26}$ –8.6 (*c* 1.0, $CHCl_3$); R_f 0.52 (toluene-ethyl acetate 2:1); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 3.57$ (s, 3H, 6-OMe), 3.87 (s, 3H, COOMe), 3.89 (dd, 1H, $J_{4',4''} = 10.1$ Hz, $J_{4',4a} = 10.1$ Hz, H-4′), 4.09 (ddd, 1H, $J_{4a,10b} = 9.1$ Hz, $J_{4a,4''} = 4.6$ Hz, H-4a), 4.36 (dd, 1H, H-4″), 4.49 (d, 1H, H-10b), 5.12 (s, 1H, H-6), 5.66 (s, 1H, H-2), 7.37–7.52 (m, 5H, Ph), 8.26 (s, 1H, H-10); ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 52.8$ (COO*C*H_3), 57.0 (6-OMe), 64.5 (C-4a), 68.7 (C-4), 73.3 (C-10b), 94.9 (C-6), 102.3 (C-2), 113.7 (C-10a), 117.7 (C-9), 126.3, 128.4, 129.5, 136.6 (Ph), 145.4 (C-10), 156.2 (C-6a), 157.9 (C-8), 163.2 (*C*OOMe); MS (EI), *m*/*z*: 374 $[M]^+$.

Anal. Calcd for $C_{19}H_{18}O_8$: C, 60.96; H, 4.85. Found: C, 60.77; H, 4.85.

Ethyl (2*R*,4a*R*,6*S*,10b*S*)-4a,6,8,10b-tetrahydro-6-methoxy-8-oxo-2-phenyl-4*H*-pyrano[3′,2′:4,5]pyrano[3,2-*d*][1,3]dioxine-9-carboxylate (3). A mixture of **1** (0.322 g, 1.0 mmol), diethyl malonate (0.160 g, 1.0 mmol), and K_2CO_3 (0.150 g, 1.1 mmol) in anhydrous DMF (20 mL) was stirred at rt for 120 hr (TLC monitoring). The mixture was then treated with saturated aqueous $NaHSO_4$ solution, extracted, washed, dried, concentrated, and coevaporated as described for the preparation of **2**. After purification by column chromatography ($CHCl_3$) and recrystallization from ethanol, pure **3** (0.166 g, 43%) was obtained as white needles; m.p. 150–152°C; $[\alpha]_D^{24}$ –15.6 (*c* 1.0, $CHCl_3$); R_f 0.32 ($CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 1.33$ (t, 3H, $J_{CH_2CH_3} = 7.0$ Hz, OCH_2CH_3), 3.57 (s, 1H, 6-OMe), 3.89 (dd, 1H, $J_{4',4a} = 10.1$ Hz, $J_{4',4''} = 10.4$ Hz, H-4′), 4.09 (ddd, 1H, $J_{4a,10b} = 8.8$ Hz, $J_{4a,4''} = 4.6$ Hz, H-4a), 4.35 (m, 3H, H-4″, OCH_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, $CDCl_3$): $\delta = 14.2$ (OCH_2CH_3), 57.0 (6-OMe), 62.0 (OCH_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, 128.4, 129.5, 136.7 (Ph), 144.8 (C-10), 156.2 (C-6a), 157.7 (C-8), 162.7 (*C*OOEt); MS (CI, *iso*-butane), *m*/*z*: 389 $[M + H]^+$.

Anal. Calcd for $C_{20}H_{20}O_8$: C, 61.85; H, 5.19. Found: C, 61.85; H, 5.08.

(2*R*,4a*R*,6*S*,10b*S*)-9-Acetyl-4,4a,7,10b-tetrahydro-6-methoxy-2,7-diphenyl-[1,3]dioxino[4′,5′:5,6]pyrano[3,4-*b*]pyridin-8(6*H*)-one (4). 3-Oxo-*N*-phenylbutyramide (0.175 g, 1.5 mmol), K_2CO_3 (0.150 g, 1.1 mmol), and 18-crown-6

(0.10 g) were added to a solution of **1** (0.322 g, 1.0 mmol) in anhydrous DMF (20 mL). After stirring at rt for 70 hr (TLC monitoring), the mixture was treated with saturated aqueous $NaHSO_4$ solution, extracted, washed, dried, concentrated, and coevaporated as described for the preparation of **2**. Purification by column chromatography (toluene-ethyl acetate 2:1) and recrystallization from ethanol yielded **4** (0.121 g, 28%) as white needles; m.p. 157–160°C; $[\alpha]_D^{25} + 4.4$ (*c* 1.0, $CHCl_3$); R_f 0.40 (toluene-ethyl acetate 2:1); ^1H NMR (250 MHz, $CDCl_3$): $\delta = 2.65$ (s, 3H, COMe), 2.85 (s, 3H, 6-OMe), 3.88 (dd, 1H, $J_{4',4''} = 10.1$ Hz, $J_{4',4a} = 10.1$ Hz, H-4′), 4.16 (ddd, 1H, $J_{4a,4''} = 4.6$ Hz, H-4a), 4.31 (dd, 1H, H-4″), 4.56 (d, 1H, $J_{10b,4a} = 9.2$ Hz, H-10b), 4.79 (s, 1H, H-6), 5.72 (s, 1H, H-2), 7.13–7.36 (m, 5H, 7-Ph), 7.38–7.59 (m, 5H, 2-Ph), 8.34 (s, 1H, H-10); ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 30.9$ (CO*C*H_3), 56.0 (6-OMe), 63.8 (C-4a), 68.9 (C-4), 74.1 (C-10b), 95.0 (C-6), 102.2 (C-2), 113.6 (C-10a), 128.6 (C-9), 126.3, 128.3, 129.4, 136.9 (2-Ph), 126.4, 129.3, 130.5, 136.6 (7-Ph), 139.8 (C-10), 144.7 (C-6a), 161.4 (C-8), 197.3 (*C*OCH$_3$); MS (CI, *iso*-butane), *m/z*: 434 $[M + H]^+$.

Anal. Calcd for $C_{25}H_{23}NO_6$: C, 69.27; H, 5.35; N, 3.23. Found: C, 69.33; H, 5.51; N, 3.24.

(2*R*,4a*R*,6*S*,10b*S*)-9-Acetyl-4,4a,7,10b-tetrahydro-6-methoxy-7-(*p*-methoxyphenyl)-2-phenyl[1,3]dioxino[4′,5′:5,6]pyrano[3,4-*b*]pyridin-8(6*H*)-one (5). *N*-(4-Methoxy-phenyl)-3-oxo-butyramide (0.248 g, 1.2 mmol), K_2CO_3 (0.150 g, 1.1 mmol), and 18-crown-6 (0.10 g) were added to a solution of **1** (0.322 g, 1.0 mmol) in anhydrous DMF (20 mL). After stirring at rt for 35 hr (TLC monitoring), the mixture was treated with saturated aqueous $NaHSO_4$ solution, extracted, washed, dried, concentrated, and coevaporated as described for the preparation of **2**. During the course of reaction at first two new spots were visible in TLC, but at the end of the reaction time only one of them was present. Purification by column chromatography (toluene-ethyl acetate 2:1) and recrystallization from ethanol yielded **5** (0.175 g, 38%) as light yellow needles; mp 258–260°C; $[\alpha]_D^{23}$ –4.0 (*c* 1.0, $CHCl_3$); R_f 0.43 (toluene-ethyl acetate 2:1); ^1H NMR (250 MHz, $CDCl_3$): $\delta = 2.65$ (s, 3H, COMe), 2.94 (s, 3H, 6-OMe), 3.86 (s, 3H, *p*-C*H*$_3$OC$_6$H$_4$), 3.88 (dd, 1H, $J_{4',4''} = 10.1$ Hz, $J_{4',4a} = 10.1$ Hz, H-4′), 4.16 (ddd, 1H, $J_{4a,4''} = 4.6$ Hz, $J_{4a,10b} = 9.2$ Hz, H-4a), 4.32 (dd, 1H, H-4″), 4.55 (d, 1H, H-10b), 4.82 (s, 1H, H-6), 5.72 (s, 1H, H-2), 6.98–7.22 (m, 4H, *p*-CH$_3$OC$_6$*H*$_4$), 7.27–7.58 (m, 5H, Ph), 8.32 (s, 1H, H-10); ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 30.9$ (CO*C*H$_3$), 55.6 (*p*-*C*H$_3$OC$_6$H$_4$), 56.2 (6-OMe), 63.8 (C-4a), 69.0 (C-4), 74.2 (C-10b), 95.1 (C-6), 102.2 (C-2), 113.4 (C-10a), 114.2, 115.1, 127.7, 128.9, 131.5, 161.7 (*p*-CH$_3$O*C*$_6$H$_4$), 126.3, 128.3, 129.3, 136.9 (Ph), 128.5 (C-9), 139.7 (C-10), 145.2 (C-6a), 160.0 (C-8), 197.4 (*C*OCH$_3$); MS (CI, *iso*-butane), *m/z*: 464 $[M + H]^+$.

Anal. Calcd for $C_{26}H_{25}NO_7$: C, 67.38; H, 5.44; N, 3.02. Found: C, 67.31; H, 5.46; N, 3.01.

(2*R*,4a*R*,6*S*,10b*S*)-9-Acetyl-4,4a,7,10b-tetrahydro-6-methoxy-7-(*o*-methylphenyl)-2-phenyl[1,3]dioxino[4′,5′:5,6]pyrano[3,4-*b*]pyridin-8(6*H*)-one (6). 3-Oxo-*N*-*o*-tolyl-butyramide (0.248 g, 1.2 mmol), K_2CO_3 (0.150 g, 1.1 mmol), and 18-crown-6 (0.10 g) were added to a solution of **1** (0.322 g, 1.0 mmol) in anhydrous DMF (20 mL). After stirring at rt for 24 hr (TLC monitoring), the mixture was treated with saturated aqueous $NaHSO_4$ solution, extracted, washed, dried, concentrated, and coevaporated as described for the preparation of **2**. During the course of reaction at first two new spots were visible in TLC, but at the end of reaction time only one of them was present. Purification by column chromatography (toluene-ethyl acetate 2:1) yielded **6** (0.256 g, 57%) as a light yellow syrup, which could be transformed into an amorphous solid by grinding; m.p. 127–131°C; $[\alpha]_D^{23} + 131.2$ (*c* 1.0, $CHCl_3$); R_f 0.52 (toluene-ethyl acetate 2:1); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 2.13$ (s, 3H, *o*-CH_3C$_6$H$_4$), 2.65 (s, 3H, COMe), 2.77 (s, 3H, 6-OMe), 3.87 (dd, 1H, $J_{4',4''} = 10.1$ Hz, H-4′), 4.12 (ddd, 1H, $J_{4a,4'} = 9.8$ Hz, H-4a), 4.29 (dd, 1H, $J_{4'',4a} = 4.6$ Hz, H-4″), 4.55 (d, 1H, $J_{10b,4a} = 9.5$ Hz, H-10b), 4.88 (s, 1H, H-6), 5.72 (s, 1H, H-2), 7.03–7.56 (m, 9H, Ph, *o*-CH$_3$C$_6$*H*$_4$), 8.34 (s, 1H, H-10); ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 17.8$ (*o*-*C*H$_3$C$_6$H$_4$), 30.8 (CO*C*H$_3$), 56.1 (6-OMe), 63.8 (C-4a), 68.9 (C-4), 74.0 (C-10b), 95.1 (C-6), 102.1 (C-2), 113.8 (C-10a), 126.2, 126.8, 129.2, 131.2, 136.1, 137.9 (*o*-CH$_3$*C*$_6$H$_4$), 126.3, 128.3, 129.4, 136.9 (Ph), 128.4 (C-9), 139.7 (C-10), 144.6 (C-6a), 160.4 (C-8), 197.3 (*C*OCH$_3$); MS (CI, *iso*-butane), *m/z*: 448 $[M + H]^+$.

Anal. Calcd for $C_{26}H_{25}NO_6$: C, 69.79; H, 5.63; N, 3.13. Found: C, 69.79; H, 5.66; N, 3.14.

(2*R*,4a*R*,6*S*,10b*S*)-4a,6,8,10b-Tetrahydro-6-methoxy-8-oxo-2-phenyl-pyrano-4*H*-[3′,2′:4,5]pyrano[3,2-*d*][1,3]dioxine-9-carboxamide (7). Method A: K_2CO_3 (0.150 g, 1.1 mmol) was added at 0°C to a solution of **1** (0.322 g, 1.0 mmol) and malononitrile (0.079 g, 1.2 mmol) in anhydrous DMF (15 mL). After stirring at this temperature for 3 hr TLC (toluene-ethyl acetate 2:1) indicated only one product at the start. As result of workup according to the procedure described for the preparation of **2**, this start product was transformed into one with an R_f value of 0.29. Purification by column chromatography (toluene-ethyl acetate 2:1) and recrystallization from ethanol gave **7** (0.067 g, 19%) as white needles.

Method B: Compound **1** (0.322 g, 1.0 mmol), cyanoacetamide (0.093 g, 1.1 mmol), and K_2CO_3 (0.150 g, 1.1 mmol) were stirred in anhydrous DMF (15 mL) at room temperature for 24 hr. In TLC (toluene-ethyl acetate 2:1) only one product appeared at the start. As result of workup according to the procedure described for the preparation of **2**, this start product was transformed into one with an R_f value of 0.29 (toluene-ethyl acetate 2:1). Recrystallization of the solid raw material from ethanol provided **7** (0.096 g, 27%) as white needles; m.p. 225–228°C; R_f 0.29 (toluene-ethyl acetate 2:1); ^{1}H NMR

(250 MHz, $CDCl_3$): $\delta = 1.72$ (s, 2H, H_2O), 3.59 (s, 3H, OMe), 3.90 (dd, 1H, $J_{4',4''} = 10.4$ Hz, $J_{4',4a} = 10.1$ Hz, H-4′), 4.10 (ddd, 1H, $J_{4a,4''} = 4.6$ Hz, H-4a), 4.37 (dd, 1H, H-4″), 4.52 (d, 1H, $J_{10b,4a} = 9.1$ Hz, H-10b), 5.17 (s, 1H, H-6), 5.67 (s, 1H, H-2), 5.98 (b, 1H, NH), 7.37–7.51 (m, 5H, Ph), 8.35 (b, 1H, NH), 8.62 (H-10); ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 57.0$ (OMe), 64.5 (C-4a), 68.7 (C4), 73.3 (C-10b), 94.8 (C-6), 102.3 (C-2), 115.2 (C-10a), 118.7 (C-9), 145.5 (C-10), 156.8 (C-6a), 160.8 (C-8), 162.7 ($CONH_2$); MS (CI, *iso*-butane), m/z: 360 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{21}NO_9$ ($C_{18}H_{17}NO_7 + 2\,H_2O$): C, 54.68; H, 5.35; N, 3.54. Found: C, 54.32; H, 5.14; N, 3.69.

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