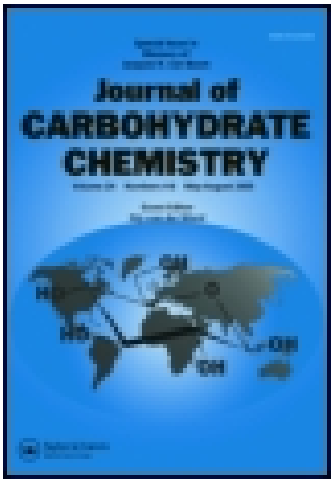

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SYNTHESIS OF 2-*C*- AND 3-*C*-ARYL PYRANOSIDES

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ABSTRACT

Lithium diphenylcuprate treatment of methyl 2,3-anhydro-4,6-*O*-benzylidene-D-pyranosides in which the anomeric substituent and the three-membered rings are *cis* oriented furnished the expected *trans*-diaxial opening products. When the relationship between the anomeric group and the epoxide was *trans*, the same experimental conditions led only to recovered starting material. Cyano cuprates of the type $R_2CuCNLi_2$ added stereoselectively to carbohydrate ketones at C-2 and C-3 from the opposite side relative to the anomeric substituent.

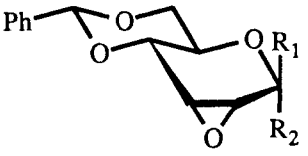
INTRODUCTION

In connection with a project aimed at synthesizing biologically active hydroxylated and polyhydroxylated analogues of the recently discovered epibatidine,[1] we were in need of substantial amounts of 2-*C*- and 3-*C*-aryl pyranosides as chiral synthons. The obvious strategy appeared to be the stereo- and regioselective opening, by an appropriate aryllithium, of the three-membered rings of the readily available methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D- and β-D-pyranosides of *allo* and *manno* configurations.

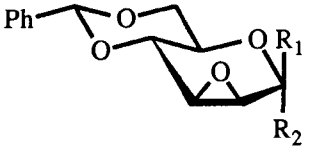
RESULTS AND DISCUSSION

Previous studies in this field were extensive with alkyllithium.[2,3] However, with aryllithium[4] they were scarce and furnished quite surprising results. In the 1950's Richards reported that methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside (**2**) reacting with diphenylmagnesium led to a 2-deoxy-2-*C*-phenyl-α-D-glucopyranoside corresponding to a *trans*-diequatorial product (74%).[5]

Instead of trying to reproduce Richard's results, we decided to treat both epoxides **1** and **2** with phenyllithium. The former, in different solvents and adding sometimes various amounts of lithium salts, afforded in low yield (from 7 to 21%) 4,6-*O*-benzylidene-1,2-dideoxy-2-*C*-phenyl-D-*ribo*-hex-1-enopyranose (**3**), corresponding to a *syn*-elimination. Using in one experiment a great excess of lithium bromide (10 equiv)

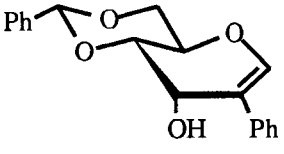


1 R_1 = H; R_2 = OMe
5 R_1 = OMe; R_2 = H



2 R_1 = H; R_2 = OMe
6 R_1 = OMe; R_2 = H

methyl 4,6-*O*-benzylidene-2-deoxy-2-bromo-α-D-altropyranoside (**4**) was also isolated (32%). The manno-epoxide **2** in all the experiments was only demolished.



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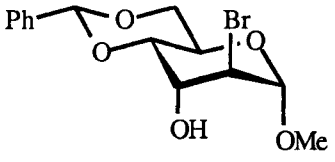
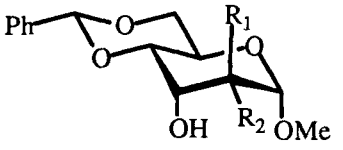


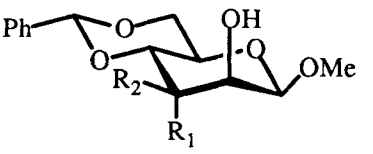
4

Upon these disappointing results, we investigated the action of lithium diaryl-cuprates[3,4,6] on four epoxides: **1**, **2**, **5**, **6**. The preparation of these epoxides followed well-established literature procedures.[7] However, access to **2** was found extremely advantageous by treating the 2-*O*-tosylate of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside under microwave irradiation (100 W) at 100 °C for 6 minutes in the presence of Al_2O_3/KOH : 3/1 (2 equiv). Under these conditions, the required manno-epoxide **2** was obtained in nearly quantitative yields, considerably improving the preparation of this important starting material. Without microwave irradiation but under exactly the same experimental conditions, the required epoxide was obtained only in 25% yield.

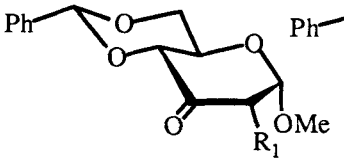
Treatment of **1** and **6** with lithium diphenylcuprate in ether at 0 °C gave the expected *trans*-diaxial products **7** (72%) and **8** (80%) respectively. However, unfortunately, from **2** and **5**, in which the relationship between the three-membered ring and the anomeric substituent is *trans*, only the starting epoxide was recovered. This is the result of the unfavorable steric interaction between the anomeric substituent and the phenyl group: 1,3-diaxial and 1,2-*cis*-gauche in the expected products, respectively.



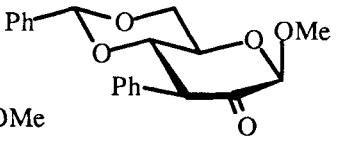
7 R_1 = Ph ; R_2 = H
11 R_1 = H ; R_2 = Ph



8 R_1 = Ph ; R_2 = H
12 R_1 = H ; R_2 = Ph



9 R_1 = Ph
13 R_1 = H



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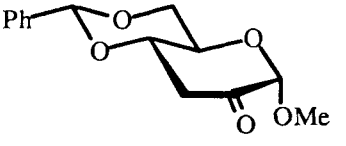
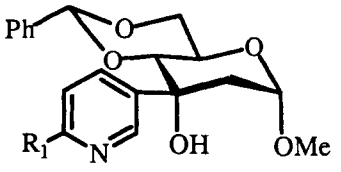


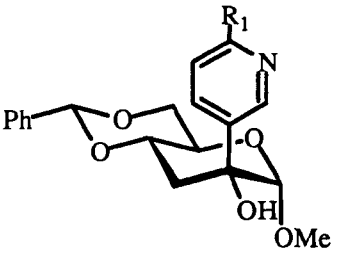
14

The two *altro* configured products **7** and **8** were submitted to sequential oxidation of their hydroxyl group by pyridinium chlorochromate in dichloromethane, followed by base catalyzed isomerisation of the *C*-phenyl substituents into keto derivatives **9** and **10**. Then, these ketones were reduced at 0 °C by sodium borohydride in a mixture of *N,N'*-dimethylformamide/methanol to the corresponding α-*allo* **11** and β-*manno* **12** alcohols in very good overall yields of 83% and 84% from **7** and **8**, respectively.

We were also interested in synthesizing 2-*C*- and 3-*C*-pyridyl pyranosides as well as 2-*C*- and 3-*C*-(2'-chloro)pyridyl pyranosides substituted in the *meta* position with respect to the nitrogen atom of the heteroaromatic ring in connection with epibatidine precursors. 2-Chloro-5-iodopyridine was prepared as described,[8] while commercial 3-bromopyridine was used for the former type of substitution. As advocated by previous investigators,[6] higher order cyano cuprates of general formula $R_2CuCNLi_2$, more economic in such reactions because of the number of equivalents of cuprate used, were prepared from 2 equiv of the appropriate heteroaromatic compounds and *n*-BuLi (2 equiv) and CuCN (1.1 equiv). Although, this type of cuprate was thought to afford better yields than simple dialkyl cuprates in the opening reaction of the epoxides, the reaction failed under all attempted conditions.



15 $R_1 = Cl$
16 $R_1 = H$



17 $R_1 = Cl$
18 $R_1 = H$

Considering a different strategy for the generation of the required C-C bond, the known ketones **13** and **14** were prepared.[9] At -78 °C in ether, both ketones underwent stereoselective addition with the above mentioned dialkyl- or dialkyl-cyano cuprates. The addition took place exclusively from the upper side of the molecules yielding, respectively, **15** (82%), **16** (78%), **17** (77%) and **18** (80%). The stereochemistry of the quaternary center of the new compounds was established by analogy with our earlier results,[10] knowing that the direction of the nucleophilic attack depends on the configuration of the anomeric substituent.

Various procedures, such as radical deoxygenation[11] or treatment with SO_2Cl_2[12] may eliminate the tertiary hydroxyl group of these compounds. However, in view of our strategy, we prefer to get rid of these hydroxyl groups at a later stage of our synthesis.

CONCLUSION

In conclusion, eight new 2-*C*- or 3-*C*-aryl pyranosides, useful chiral synthons, for *C*-aryl substituted polyhydroxy cyclohexane type natural products and their analogues have been synthesized.

EXPERIMENTAL

General methods and equipment. Flash column chromatography was performed using 35-70 μ silica gel (60) purchased from S.D.S. company. TLC was run using DC-Plastikfolien, silica gel F_{254} (Schleicher and Schuell), detection by UV light (254 nm) and by heating after sulfuric acid treatment. The term "standard workup" means that the organic layer was washed with water, dried over Na_2SO_4, and filtered and the solvent was removed at reduced pressure. Mass spectra were run on an AEIMS59 for

the CI mass spectra. ^1H and ^{13}C spectra were recorded at 200 MHz and 50.33 MHz, at 250 MHz and 62.91 MHz and at 300 MHz and 75.49 MHz (Bruker WP 200, WP 250, WP 300, respectively). Tetramethylsilane was the internal standard (δ = 0.00 ppm). Carbon-13 chemical shifts for aromatic carbons agree with literature data[13] and are not given. Melting points were measured on a Reichert apparatus and are uncorrected. Optical rotations were determined with a Perkin-Elmer 241 polarimeter.

Focused microwave irradiations were carried out with a Synthewave^{TM} S402 monomode reactor from Prolabo (2450 MHz, 300 W) fitted with a stirring system of variable speed rotation, a visual control and with irradiation monitoring by a PC. *Infra*-red measurement and continual feedback temperature control were adjusted and controlled through an optical fiber.

Methyl 2,3-Anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside (2). To methyl 4,6-*O*-benzylidene-2-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside (1 g, 2.3 mmol) was added KOH/Al_2O_3 (1 : 3) (1.2 g) (KOH 4 equiv) and the mixture was irradiated under microwave conditions (temperature control, initial power 100 W, temperature limited 100 °C) for 6 min. After dilution with EtOAc, filtration and solvent evaporation, pure epoxide **2** was obtained (0.6 g, 99%).

4,6-*O*-Benzylidene-1,2-dideoxy-2-*C*-phenyl-D-*ribo*-hex-1-eno-pyranose (3). To a solution of epoxide **6** (0.39 g, 1.4 mmol) and lithium fluoride (0.2 g, 7.4 mmol) in toluene (5 mL) at 0 °C was added dropwise a solution of phenyllithium in toluene (1.8 N, 1.65 mL, 2.97 mmol). Stirring was maintained for 3 h and then the solution was refluxed for another 3 h. After the usual work-up (dilution with water, extraction with dichloromethane, separation and drying of the organic layer over sodium sulfate and concentration under reduced pressure) and chromatography of the residue using ethyl acetate/heptane (1:1), syrupy **3** (0.1 g, 21%) was isolated. $[\alpha]_D$ + 152° (c 1.0, chloroform); mass spectrum: (I.C.) *m/z* 311 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50-7.20 (m, 10H, 2 Ph), 6.85 (s, 1H, H-1), 5.70 (s, 1H, H-7), 4.75 (d, 1H, $J_{3,4}$ = 2 Hz, H-3), 4.53 (dd, 1H, $J_{5,6eq}$ = 4 Hz, J_{gem} = 9 Hz, H-6eq), 4.30 (m, 1H, H-5), 3.92 (dd, 1H, $J_{4,5}$ = 10 Hz, H-4), 3.87 (t, 1H, $J_{5,6ax} = J_{gem}$ = 9 Hz, H-6ax), 2.65 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) 143.4 (C-1), quaternary carbon of low intensity, not detected (C-2), 101.8 (C-7), 77.8 (C-4), 68.8 (C-6), 63.6 (C-3), 62.9 (C-5).

Anal. Calcd for $C_{19}H_{18}O_4$ (310.33): C, 73.53; H, 5.85. Found: C, 73.81; H, 5.99.

Methyl 4,6-*O*-Benzylidene-2-bromo-2-deoxy-α-D-altropyranoside (4). To a solution of epoxide **6** (0.44 g, 1.68 mmol) and lithium bromide (1.46 g, 16.8 mmol) in toluene (20 mL) at 0 °C was added dropwise a solution of phenyllithium in

toluene (1.8 N, 1.5 mL, 3.36 mmol). Stirring was maintained for 1 h then the solution was refluxed for another 3 h. After the usual work-up and chromatography of the residue using ethyl acetate/heptane (1:1), syrupy **3** (0.07 g, 13%) and syrupy **4** (0.18 g, 32%) were isolated: **(4)** $[\alpha]_D$ + 59° (*c* 1.0, chloroform); mass spectrum: (I.C.) *m/z* 346 $(M+H)^+$; ^1H NMR (250 MHz, $CDCl_3$) δ 7.60-7.30 (m, 5H, Ph), 5.63 (s, 1H, H-7), 4.90 (s, 1H, H-1), 4.40-4.20 (m, 4H, H-3, 5, 6ax and 6eq), 4.18 (d, 1H, $J_{2,3}$ = 1 Hz, H-2), 3.83 (dd, 1H, $J_{3,4}$ = 3 Hz, $J_{4,5}$ = 8 Hz, H-4), 3.40 (s, 3H, OMe), 3.10 (s, 1H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 102.3 (C-7), 101.7 (C-1), 74.9 (C-4), 69.7 (C-3), 69.0 (C-6), 58.5 (C-5), 56.0 (OMe), 46.9 (C-2).

Anal. Calcd for $C_{14}H_{17}BrO_5$ (345.192): C, 48.71; H, 4.96; Br, 23.15. Found: C, 48.92; H, 5.07; Br, 23.52.

Methyl 4,6-*O*-Benzylidene-2-deoxy-2-*C*-phenyl-α-D-altropyranoside (7). To a suspension of CuBr (0.55 g, 3.8 mmol) in anhydrous ether (30 mL), under a nitrogen atmosphere at 0 °C was added a solution of phenyllithium in toluene (1.8 N, 4.22 mL, 7.6 mmol). To this mixture was added slowly epoxide **1** (0.5 g, 1.9 mmol) in anhydrous ether (5 mL). Stirring was maintained for 4 h and after the usual work-up the residue was recrystallized from ethanol, giving pure **7** (0.47 g, 72%): mp 167-168 °C; $[\alpha]_D$ + 75° (*c* 1.0, chloroform); mass spectrum: (I.C.) *m/z* 343 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50-7.20 (m, 10H, 2 Ph), 5.53 (s, 1H, H-7), 5.10 (d, 1H, $J_{1,2}$ = 1 Hz, H-1), 4.40 (dd, 1H, $J_{5,6eq}$ = 4 Hz, J_{gem} = 9 Hz, H-6eq), 4.38 (m, 1H, H-5), 4.13 (d, 1H, $J_{3,4}$ = 2 Hz, H-3), 3.90 (t, 1H, $J_{5,6ax}$ = J_{gem} = 9 Hz, H-6ax), 3.80 (dd, 1H, 52 (m, 1H, H-2), 3.50 (s, 3H, OMe), 3.30 (d, 1H, $J_{3,OH}$ = 7 Hz, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 102.3 (C-7), 101.3 (C-1), 75.7 (C-4), 71.5 (C-3), 69.5 (C-6), 58.6 (C-5), 55.7 (OMe), 51.0 (C-2).

Anal. Calcd for $C_{20}H_{22}O_5$ (342.38): C, 70.16; H, 6.48. Found: C, 70.28; H, 6.47.

Methyl 4,6-*O*-Benzylidene-3-deoxy-3-*C*-phenyl-β-D-altropyranoside (8). This compound was obtained (80%) from **6** as described for the preparation of **7** from **1**: mp 167-168 °C; $[\alpha]_D$ + 27° (*c* 1.0, chloroform); mass spectrum: (I.C.) *m/z* 343 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$) δ 7.60-7.20 (m, 10H, 2 Ph), 5.58 (s, 1H, H-7), 4.80 (d, 1H, $J_{1,2}$ = 1 Hz, H-1), 4.40 (dd, 1H, $J_{3,4}$ = 6 Hz, $J_{4,5}$ = 10 Hz, H-4), 4.33 (dd, 1H, $J_{5,6eq}$ = 4 Hz, J_{gem} = 10 Hz, H-6eq), 4.25 (d, 1H, $J_{2,3}$ = 2 Hz, H-2), 4.05 (m, 1H, H-5), 3.83-3.75 (m, 2H, H-3, H-6ax), 3.55 (s, 3H, OMe), 2.88 (m, 1H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 102.3 (C-7), 99.4 (C-1), 76.1 (C-4), 73.1 (C-2), 69.6 (C-6), 64.9 (C-5), 56.7 (OMe), 46.6 (C-3).

Anal. Calcd for $C_{20}H_{22}O_5$ (342.38): C, 70.16; H, 6.48. Found: C, 69.91; H, 6.65.

Methyl 4,6-*O*-Benzylidene-2-deoxy-2-*C*-phenyl-α-D-*ribo*-hexos-3-ulopyranoside (9). To a mixture of pyridinium chlorochromate (1 g, 4.6 mmol) and 3 Å molecular sieves (1.17 g) in anhydrous dichloromethane (6 mL) was added **7** (0.4g, 1.17 mmol). Stirring was applied at room temperature for 4 h and followed by filtration on silica gel. After concentration, the crude residue (0.35 g), already partially isomerized as shown by its ^{1}H NMR spectrum, although homogeneous on TLC, was added to a solution of ethanol (5.2 mL) containing dichloromethane (0.5 mL) and triethylamine (0.3 mL). Stirring was applied for 1 h and after the usual work-up the intermediate 3-ulose, epimerized at C-2, **9** was isolated (0.37 g, 94%) as crystals from methanol: mp 167-168 °C; $[\alpha]_D$ + 202° (*c* 1.0, chloroform); mass spectrum: (I.C.) *m/z* 341 $(M+H)^+$; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.70-7.30 (m, 10H, 2 Ph), 5.65 (s, 1H, H-7), 5.10 (d, 1H, $J_{1,2}$ = 4 Hz, H-1), 4.40 (d, 1H, $J_{4,5}$ = 10 Hz, H-4), 4.45-4.25 (m, 2H, H-5, H-6eq), 4.08 (d, 1H, H-2), 3.98 (t, 1H, $J_{5,6ax} = J_{gem}$ = 10 Hz, H-6ax), 3.35 (s, 3H, OMe); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 196.4 (C-3), 104.5 (C-7), 102.2 (C-1), 83.2 (C-4), 69.7 (C-6), 66.1 (C-5), 61.0 (C-2), 55.5 (OMe).

Anal. Calcd for $C_{20}H_{20}O_5$ (340.38): C, 70.58; H, 5.92. Found: C, 70.54; H, 5.96.

Methyl 4,6-*O*-Benzylidene-3-deoxy-3-*C*-phenyl-β-D-*arabino*-hexos-2-ulopyranoside (10). This compound was prepared in a yield of 89 % from **8** in the same way as described for the preparation of **9** from **7**: mp 209-210 °C; $[\alpha]_D$ - 90° (*c* 1.0, chloroform); mass spectrum: (I.C.) *m/z* 341 $(M+H)^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.20 (m, 10H, 2 Ph), 5.48 (s, 1H, H-7), 4.83 (s, 1H, H-1), 4.50 (dd, 1H, $J_{5,6eq}$ = 5 Hz, J_{gem} = 10 Hz, H-6eq), 4.28 (dd, 1H, $J_{3,4}$ = 11 Hz, $J_{4,5}$ = 10 Hz, H-4), 3.98 (dt, 1H, $J_{5,6ax}$ = 10 Hz, H-5), 3.87 (t, 1H, H-6ax), 3.81 (d, 1H,, H-3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.9 (C-2), 101.7 (C-7), 101.2 (C-1), 80.0 (C-4), 69.6 (C-5), 69.4 (C-6), 60.1 (C-3), 56.7 (OMe).

Anal. Calcd for $C_{20}H_{20}O_5$ (340.38): C, 70.58; H, 5.92. Found: C, 70.58; H, 5.76.

Methyl 4,6-*O*-Benzylidene-2-deoxy-2-*C*-phenyl-α-D-allopyranoside (11). The ketone **9** (0.2 g, 0.59 mmol) was dissolved in a mixture of DMF (2 mL) and methanol (3 mL) and sodium borohydride (0.11 g, 2.9 mmol) was added to the solution at 0 °C. Stirring was applied for 3 h and then the usual work-up gave, after filtration on a column of silica gel, pure **11** (0.185 g, 92%): mp 115 °C; $[\alpha]_D$ + 74° (*c* 1.0, chloroform); mass spectrum: (I.C.) *m/z* 343 $(M+H)^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.20 (m, 10H, 2 Ph), 5.60 (s, 1H, H-7), 4.90 (d, 1H, $J_{1,2}$ = 3 Hz, H-1), 4.40-4.20 (m, 3H, H-3, H-5, H-6eq), 3.82 (t, 1H, $J_{5,6ax} = J_{gem}$ = 10 Hz, H-6ax), 3.66 (dd, 1H, $J_{3,4}$ = 3 Hz, $J_{4,5}$ = 10 Hz, H-4), 3.35 (s, 3H, OMe), 3.10 (t, 1H, $J_{2,3} = J_{3,4}$

= 3 Hz, H-2); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 102.0 (C-7), 101.7 (C-1), 80.4 (C-4), 69.2 (C-6), 69.1 (C-3), 58.4 (C-5), 55.8 (OMe), 48.6 (C-2).

Anal. Calcd for $C_{20}H_{22}O_5$ (342.38): C, 70.16; H, 6.48. Found: C, 70.04; H, 6.55.

Methyl-4,6-*O*-Benzylidene-3-deoxy-3-*C*-phenyl-β-D-mannopyranoside (12). This compound was prepared in a yield of 85 % from **10** in the same way as described for the preparation of **11** from **9**: mp 137 °C; $[\alpha]_D$ - 133° (*c* 1.0, chloroform); mass spectrum: (I.C.) *m/z* 343 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40-7.10 (m, 10H, 2 Ph), 5.62 (s, 1H, H-7), 4.68 (d, 1H, $J_{1,2}$ = 1 Hz, H-1), 4.44 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 10 Hz, H-4), 4.35 (dd, 1H, $J_{5,6eq}$ = 4 Hz, J_{gem} = 10 Hz, H-6eq), 4.08 (t, 1H, $J_{1,2}$ = $J_{2,3}$ = 1 Hz, H-2), 3.94 (t, 1H, $J_{5,6ax}$ = J_{gem} = 10 Hz, H-6ax), 3.63 (m, 1H, H-5), 3.58 (s, 3H, OMe), 3.13 (dd, 1H, $J_{2,3}$ = 1 Hz, $J_{3,4}$ = 10 Hz, H-3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 102.2 (C-7), 100.8 (C-1), 74.7 (C-4), 71.2 (C-2), 69.4 (C-5), 67.9(C-6), 55.8 (OMe), 48.9 (C-3).

Anal. Calcd for $C_{20}H_{22}O_5$ (342.38): C, 70.16; H, 6.48. Found: C, 70.14; H, 6.50.

Methyl 4,6-*O*-Benzylidene-2-deoxy-3-*C*-[2'-chloro-5'-pyridyl]-α-D-ribopyranoside (15). To a solution of 2-chloro-5-iodopyridine (1.416 g, 5.8 mmol) in ether (25 mL) was added at -78 °C *n*-BuLi in heptane (3.7 mL, 1.6 N). After stirring at -78 °C for 30 min CuCN (0.3 g, 3.2 mmol) was added and stirring was continued for another 30 min at -78 °C. Then, ketone **13** (0.78 g, 2.9 mmol) was introduced into the mixture. The latter was stirred at -78 °C for another 6 h and the usual work-up gave a residue which was crystallized from ethyl acetate/heptane affording pure crystalline **15** (0.91 g, 82 %): mp 145 °C; $[\alpha]_D$ + 14° (*c* 1.0, chloroform); mass spectrum: (I.C.) *m/z* 378-380 $(M+H)^+$; ^1H NMR (250 MHz, $CDCl_3$) δ 8.50 (d, 1H, $J_{2',4'}$ = 2 Hz, H-2'), 7.85 (dd, 1H, $J_{4',5'}$ = 7 Hz, H-4'), 7.30 (d, 1H, H-5'), 7.30-7.20 (m, 5H, 1 Ph), 5.55 (s, 1H, H-7), 4.90 (s, 1H, H-1), 4.40-4.20 (m, 3H, H-6eq, H-5, OH), 3.92 (d, 1H, $J_{4,5}$ = 10 Hz, H-4), 3.85 (t, 1H, J_{gem} = $J_{5,6ax}$ = 10 Hz, H-6ax), 3.43 (s, 3H, OMe), 2.18 (s, 2H, H-2ax, H-2eq); ^{13}C NMR (75 MHz, $CDCl_3$) δ 101.9 (C-7), 98.5 (C-1), 81.6 (C-4), 71.2 (C-3), 69.1 (C-6), 60.1 (C-5), 55.5 (OMe), 42.3 (C-2).

Anal. Calcd for $C_{19}H_{20}O_5NCl$ (377.83): C, 60.40; H, 5.34; N, 3.71; Cl, 9.38. Found: C, 60.21; H, 5.37; N, 3.61; Cl, 9.42.

Methyl 4,6-*O*-Benzylidene-2-deoxy-3-*C*-[3'-pyridyl]-α-D-ribo-pyranoside (16). To a solution of 3-bromopyridine (0.3 mL, 3 mmol) in ether (25 mL) was added at -78 °C *n*-BuLi in heptane (1.9 mL, 1.6 N). After stirring at -78 °C for 30 min CuBr (0.22 g, 6 mmol) was added and stirring was continued for another 40 min at -78 °C. Then, ketone **13** (0.2 g, 0.75 mmol) was introduced into the mixture. The latter was

stirred at -78 °C for another 6 h and the usual work-up gave a residue which was chromatographed on silica gel using ethyl acetate/heptane (3:7) giving pure crystalline **16** (0.20 g, 78 %): mp 126 °C; $[\alpha]_D$ + 54° (*c* 1.0, chloroform); mass spectrum: (I.C.) *m/z* 344 $(M+H)^+$; ^1H NMR (250 MHz, $CDCl_3$) δ 8.78 (d, 1H, $J_{2',4'}$ = 2 Hz, H-2'), 8.48 (d, 1H, $J_{5',6'}$ = 2 Hz, H-6'), 7.90 (dd, 1H, $J_{4',5'}$ = 7 Hz, H-4'), 7.30 (dd, 1H, H-5'), 7.30-7.20 (m, 5H, Ph), 5.57 (s, 1H, H-7), 4.90 (s, 1H, H-1), 4.40 (dd, 1H, $J_{5,6eq}$ = 5 Hz, J_{gem} = 10 Hz, H-6eq), 4.35 (dt, 1H, H-5), 4.20 (s, 1H, OH); 4.00 (d, 1H, $J_{4,5}$ = 10 Hz, H-4), 3.87 (t, 1H, $J_{5,6ax}$ = J_{gem} = 10 Hz, H-6ax), 3.47 (s, 3H, OMe), 2.20 (s, 2H, H-2ax, H-2eq); ^{13}C NMR (75 MHz, $CDCl_3$) δ 101.8 (C-7), 98.6 (C-1), 81.6 (C-4), 71.3 (C-3), 69.2 (C-6), 59.9 (C-5), 55.5 (OMe), 42.6 (C-2).

Anal. Calcd for $C_{19}H_{21}O_5N$ (343.38): C, 66.46; H, 6.16; N, 4.08; Found: C, 66.17; H, 6.18; N, 4.29.

Methyl 4,6-*O*-Benzylidene-3-deoxy-2-*C*-[2'-chloro-5'-pyridyl]-α-D-ribopyranoside (17). This compound was prepared (77%) from **14** as described for the preparation of **15** from **13**: mp 136 °C; $[\alpha]_D$ + 31° (*c* 1.0, chloroform); mass spectrum: (I.C.) *m/z* 378-380 $(M+H)^+$; ^1H NMR (250 MHz, $CDCl_3$) δ 8.70 (d, 1H, $J_{2',4'}$ = 2 Hz, H-2'), 7.98 (dd, 1H, $J_{4',5'}$ = 7 Hz, H-4'), 7.40 (d, 1H, H-5'), 7.30-7.20 (m, 5H, Ph), 5.40 (s, 1H, H-7), 4.90 (s, 1H, H-1), 4.32 (dd, 1H, $J_{5,6eq}$ =5 Hz, J_{gem} = 10 Hz, H-6eq), 3.88 (dt, 1H, H-5), 3.73 (t, 1H, $J_{5,6ax}$ = J_{gem} = 10 Hz, H-6ax), 3.54 (s, 3H, OMe), 3,30 (dt, 1H, H-4), 2.27 (t, 1H, $J_{3ax,4}$ = J_{gem} = 10 Hz, H-3ax), 2.25 (d, 1H, $J_{3eq,4}$ = 4 Hz, H-3eq); ^{13}C NMR (75 MHz, $CDCl_3$) δ 101.7 (C-7), 100.6 (C-1), 74.9 (C-4), 72.1 (C-2), 69.2 (C-6), 64.6 (C-5), 55.5 (OMe), 40.8 (C-3).

Anal. Calcd for $C_{19}H_{20}O_5NCl$ (377.83): C, 60.40; H, 5.34; N, 3.71; Cl, 9.38. Found: C, 60.55; H, 5.42; N, 3.83; Cl, 9.42.

Methyl 4,6-*O*-Benzylidene-3-deoxy-2-*C*-[3'-pyridyl]-α-D-ribo-pyranoside (18). This compound was prepared (80%) from **14** as described for the preparation of **16** from **13** : mp 141 °C; $[\alpha]_D$ + 58° (*c* 1.0, chloroform); mass spectrum: (I.C.) *m/z* 344 $(M+H)^+$; ^1H NMR (250 MHz, $CDCl_3$) δ 8.94 (d, 1H, $J_{2',4'}$ = 2 Hz, H-2'), 8.55 (d, 1H, $J_{5',6'}$ = 2 Hz, H-6'), 8.00 (dd, 1H, H-4'), 7.41 (dd, 1H, $J_{4',5'}$ = 8 Hz, H-5'), 7.30-7.25 (m, 5H, Ph), 5.40 (s, 1H, H-7), 4.90 (s, 1H, H-1), 4.32 (dd, 1H, $J_{5,6eq}$ = 4 Hz, J_{gem} = 10 Hz, H-6eq), 3.90 (dt, 1H, H-5); 3.74 (t, 1H, $J_{5,6ax}$ = J_{gem} = 10 Hz, H-6ax), 3.54 (s, 3H, OMe), 3.34 (dt, 1H, H-4), 2.30 (d, 1H, $J_{3eq,4}$ = 4 Hz, J_{gem} = 10 Hz, H-3eq), 2.28 (t, 1H, $J_{3ax,4}$ = J_{gem} = 10 Hz, H-3ax); ^{13}C NMR (75 MHz, $CDCl_3$) δ 101.7 (C-7), 100.9 (C-1), 75.0 (C-4), 72.0 (C-2), 69.2 (C-6), 64.6 (C-5), 55.5 (OMe), 40.8 (C-3).

Anal. Calcd for $C_{19}H_{21}O_5N$ (343.38): C, 66.46; H, 6.16; N, 4.08; Found: C, 66.52; H, 6.24; N, 4.19.

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