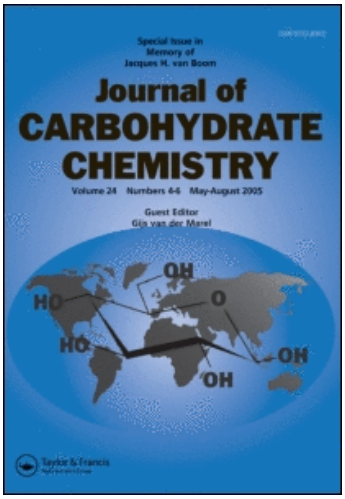

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SYNTHETIC USEFULNESS OF THE SUGAR CYCLOPENTYLIDENE KETALS

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ABSTRACT

Cyclopentylidene ketals, moderately more acid-labile than their isopropylidene analogs, offer an alternative to the latter blocking groups. They have been shown to resist a large variety of reaction conditions commonly encountered in carbohydrate chemistry.

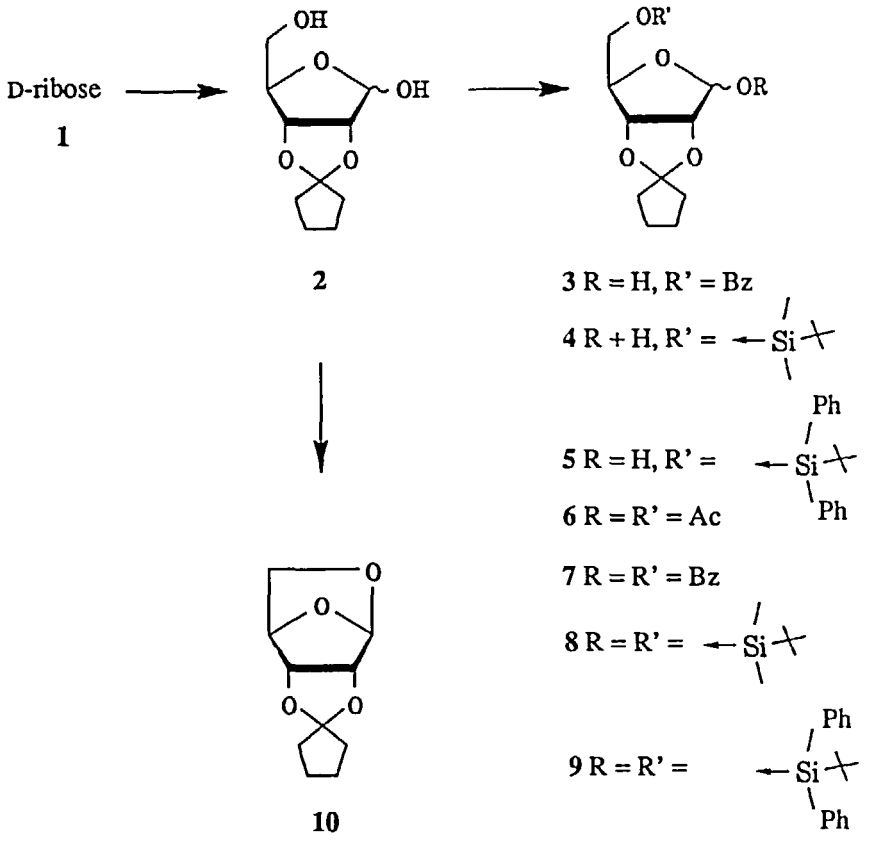
INTRODUCTION

Since their first application in nucleoside chemistry,[1] cyclopentylidene ketals have only been sporadically used in carbohydrate chemistry.[2] Their major practical characteristic consists in their acidic solvolysis being faster than that of their isopropylidene competitors. The potential drawback of the procedure comes from the relatively high boiling point of the cyclopentanone (and especially of its dimer) which renders the purification of the ketals a little more laborious when non-crystalline. This somewhat low volatility makes also the recycling of the moderately expensive ketone reagent less easy than in the case of propanone.

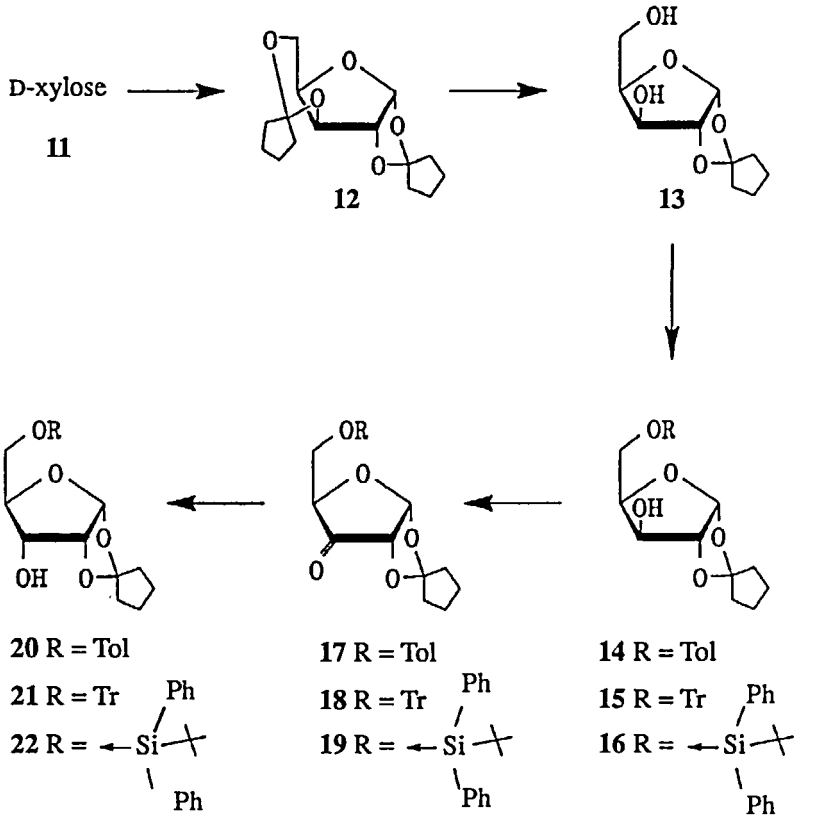
As the cyclopentylidene ketals were shown to be sufficiently stable to resist the acidic conditions of the cyanoborohydride reduction of oximes into hydroxylamines,[3] they certainly constitute useful synthetic intermediates of well-balanced solvolyzability, some novel examples of which are described below.

RESULTS AND DISCUSSION

The condensation of D-ribose with cyclopentanone in anhydrous acidic media ($CuSO_4$, H_2SO_4) yielded the 2,3-*O*-cyclopentylidene derivative **2**, which could be easily protected at its terminal position by stoichiometric amounts of benzoyl chloride, *tert*-bu-



tyldimethylchlorosilane or *tert*-butyldiphenylchlorosilane to give **3**, **4** and **5**, respectively.



Di-*O*-acylations of **2** led to **6** and to **7** while di-*O*-silylations led to **8** and **9**. Attempted distillation of **2** gave small amounts of the 1,5-anhydrosugar **10**.

The same condensation procedures ($CuSO_4$, H_2SO_4) applied to D-xylose gave the di-*O*-cyclopentylidene derivative **12** which was partially deprotected to **13** under acidic conditions (HCl, MeOH). Selective *O*-toluylation of **13** led to **14**, which was oxidized (CrO_3/pyridine) to the ketosugar **17**, reducible ($NaBH_4$, MeOH) to the ribofuranose derivative **20**. The same oxidation-reduction sequence applied to the selectively tritylated compound **15** and the 5-*O*(*tert*-butyldiphenylsilyl) xylose derivative **16**, gave the ketosugars **18** and **19** which were reduced to the ribose derivatives **21** and **22** respectively. This confirmed the easiness of the selective partial deblocking of the 3,5 or 5,6 positions[2,3] of furanoses and the ability of these ketal derivatives to survive a panel of reaction conditions often encountered in carbohydrate chemistry. After the ketalization reaction, the excess ketone was recovered in 80% yield in an almost pure form suitable for its reuse.

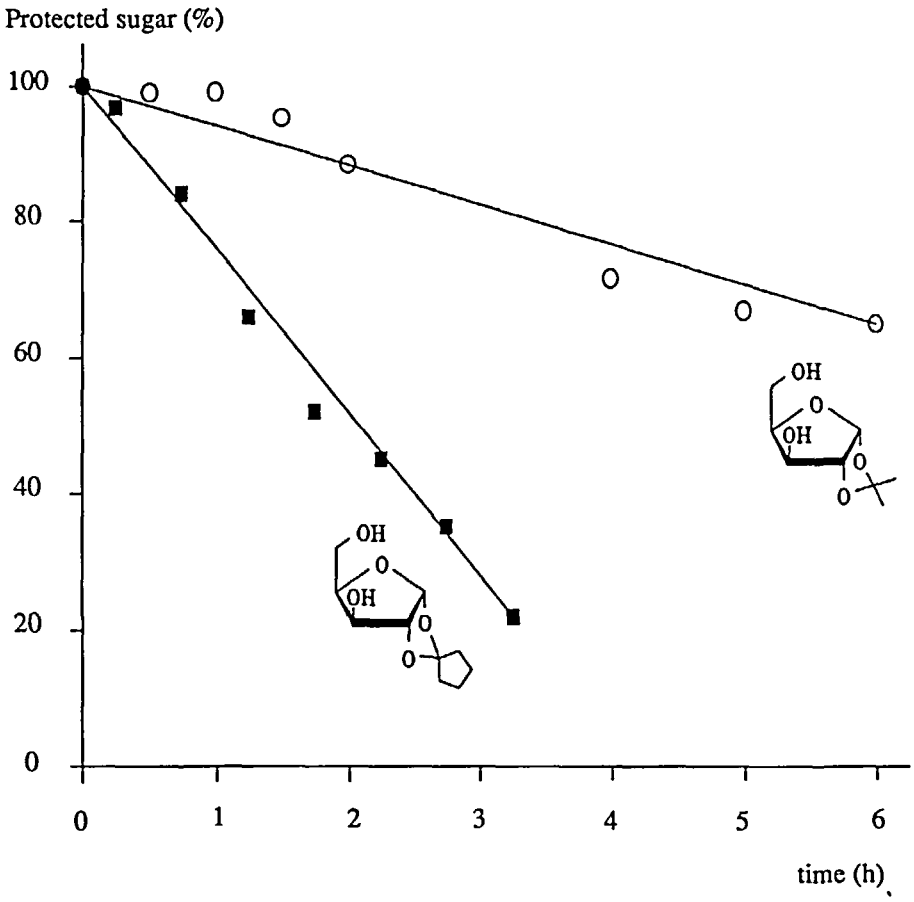


FIG. Comparative rates of methanolysis of 1,2-isopropylidene- and 1,2-*O*-cyclopentylidene- α-D-xylofuranoses.

The relative ease of deprotection by acidic methanolysis (MeOH/Dowex 50 [H^+]) of 1,2-*O*-isopropylidene-α-D-xylofuranose[4] and its cyclopentylidene analog **13** has been measured by monitoring ^1H NMR signals of **13** (H-1 and $(CH_2)_4$) and of 1,2-*O*-isopropylidene-α-D-xylofuranose (H-1 and CMe_2) (FIG.). The half-live of **13** was more than three times smaller than that of its isopropylidene congener.

EXPERIMENTAL

General Procedures.[5] Optical rotations were measured in chloroform solutions.

2,3-*O*-Cyclopentylidene-β-D-ribofuranose (2). To a solution of commercial D-ribose (10 g, 66 mmol) in dry cyclopentanone (300 mL), anhydrous cupric sulfate (12 g, 80 mmol) and concentrated sulfuric acid (1 mL) were added and the mixture stirred at room temperature for 36 h, then filtered. The filtrate was treated for 2 h with $NaHCO_3$ (10 g, 12 mmol.), concentrated to dryness and the resulting residue extracted with ether (100 mL), filtered, washed with water (3x50 mL) and dried (Na_2SO_4). Direct distillation of crude **2** failed to give the analytically pure **2**, but yielded small quantities (1 g, 9%) of the anhydrosugar **10**. Thus, for the purification of **2** we resorted to a column chromatography on silica gel (AcOEt/hexane 1:1) which gave 9.7 g (67%) of **2** as a syrup, $[\alpha]_D^{25}$ -24.1° (*c* 3.9); ν_{max}^{KBr} 3500, 1440, 1205, 1050, and 710 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 5.43 (*d*, 1 H, $J_{1,OH}$ 4 Hz, $J_{1,2}$ 0 Hz, H-1), 5.20 (*d*, 1 H, HO-1), 4.77 (*broad d*, 1 H, $J_{2,3}$ 6 Hz, $J_{3,4}$ 0.5 Hz, H-3), 4.52 (*d*, 1 H, H-2), 4.43 (*broad t*, 1 H, $J_{4,5}$ 2.3 Hz, H-4), 3.95 (*broad t*, 1 H, $J_{5,OH}$ 5 Hz, HO-5), 3.73 (*dd*, 2 H, 2H-5), 1.94 and 1.65 (*2 m*, 8 H, cyclopent.). MS: *m/z* 216 (7, $M^{+\cdot}$), 187 (90), 169 (40), 115 (20), 97 (30), 85 (45), 69 (20), and 55 (100).

Anal. Calcd for $C_{10}H_{16}O_5$ (216.24): C, 55.55; H, 7.46. Found: C, 55.35; H, 7.44.

5-*O*-Benzoyl-2,3-*O*-cyclopentylidene-β-D-ribofuranose (3). To a solution of **2** (9.7 g, 45 mmol) in pyridine (200 mL), benzoyl chloride (5.2 mL, 45 mmol) was added, and the mixture stirred at room temperature for 12 h. After removal of the pyridine by distillation the residue was dissolved in ether (100 mL) and the organic phase washed with water (3x50 mL), dried (Na_2SO_4), and concentrated to give 14 g (97%) of crude **3**. Further purification by column chromatography (AcOEt/hexane 1:1) gave 11.5 g (80%) of analytically pure **3** as a syrup, $[\alpha]_D^{24}$ -8.6° (*c* 1.2); λ_{max}^{EtOH} 203 (ε 37370), and 228 nm (17750); ν_{max}^{KBr} 3440, 1715, 1445, 1270, 1100, and 1070 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): 8.08 and 7.50 (*2 m*, 5 H, Bz), 5.54 (*d*, 1 H, $J_{1,OH}$ 3 Hz, $J_{1,2}$ 0 Hz, H-1), 4.79 (*broad d*, 1H, $J_{2,3}$ 6 Hz, $J_{3,4}$ 0.5 Hz, H-3), 4.67 (*d*, 1 H, H-2), 4.65-4.30 (*m*, 3 H, H-4 and 2 H-5), 3.22 (*d*, 1 H, HO), 1.97 and 1.71 (*2 m*, 8 H, cyclopent.). MS: *m/z* 216 (5), 187 (63), 169 (38), 97 (25), 85 (38), 69 (20), and 55 (100).

Anal. Calcd for $C_{17}H_{20}O_6$ (320.35): C, 63.74; H, 6.29. Found: C, 63.44; H, 6.37.

5-*O*-(*tert*-Butyldimethylsilyl)-2,3-*O*-cyclopentylidene-β-D-ribofuranose (4). To a solution of **2** (8.4 g, 39 mmol) in dry pyridine (200 mL), *tert*-butyldimethylchlorosilane

(5.8 g, 39 mmol) was added. After 12 h at room temperature the reaction mixture treated as usual gave after column chromatography (AcOEt/hexane 1:4) 6 g (47%) of **4** together with 1 g (6%) of **8** as a mixture of α and β isomers, syrup, $[\alpha]_D^{26}$ - 10.3 ° (*c* 1.2); ν_{max}^{KBr} 3450, 1335, 1255, 1110, and 1000 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 5.28 (*d*, 1 H, $J_{1,OH}$ 12 Hz, $J_{1,2}$ 0 Hz, H-1), 4.77 (*d*, 1 H, OH), 4.66 (*broad d*, 1 H, $J_{2,3}$ 6 Hz, $J_{3,4}$ 0.5 Hz, H-3), 4.44 (*d*, 1 H, H-2), 4.38 (*broad t*, 1 H, $J_{4,5a}$ 2 Hz, $J_{4,5b}$ 2 Hz, H-4), 3.79 (*dd*, 1 H, $J_{5a,5b}$ 11 Hz, Ha-5), 3.73 (*dd*, 1 H, Hb-5), 1.95 and 1.70 (*2 m*, 8 H, cyclopent.), 0.92 (*s*, 9 H, Me_3C), and 0.17 (*s*, 6 H, 2 MeSi). MS: *m/z* 330(3, M^+), 301 (14), 189 (12), 143 (30), 117 (46), 75 (100), and 55 (32).

Anal. Calcd for $C_{16}H_{30}O_5Si$ (330.50): C, 58.15; H, 9.15. Found: C, 57.93; H, 9.19.

5-*O*-(*tert*-Butyldiphenylsilyl)-2,3-di-*O*-cyclopentylidene-β-D-ribofuranose (5). To a solution of **2** (2 g, 9.2 mmol), in dry pyridine (100 mL), *tert*-butyldiphenylchlorosilane (9.25 mL, 13.9 mmol) was added. After 36 h at room temperature, the reaction mixture was treated as usual to give after column chromatography on silica gel (AcOEt/hexane 1:2) 1.5 g (36%) of **5** together with 0.4 g (6%) of **9** as a mixture of α and β isomers, syrup, $[\alpha]_D^{22}$ -30.0° (*c* 1.2); λ_{max}^{EtOH} 2203 (21710), 220 (14120); ν_{max}^{KBr} 1470, 1430, 1340, 1100, and 1000 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 7.70 and 7.45 (*2 m*, 10 H, Ar), 5.40 (*d*, 1 H, $J_{1,OH}$ 11 Hz, $J_{1,2}$ 0 Hz, H-1), 4.71 (*broad d*, 1 H, $J_{2,3}$ 7 Hz, $J_{3,4}$ 0.5 Hz, H-3), 4.53 (*d*, 1 H, OH), 4.53 (*d*, 1 H, H-2), 4.30 (*broad t*, 1 H, $J_{4,5a}$ 2 Hz, $J_{4,5b}$ 2 Hz, H-4), 3.82 (*dd*, 1 H, $J_{5a,5b}$ 12 Hz, Ha-5), 3.72 (*dd*, 1H, Hb-5), 1.89 and 1.80 (*2 m*, 8 H, cyclopent.), and 1.05 (*s*, 9 H, Me_3C). MS: *m/z* 199 (66), 187 (44), 163 (48), 139 (34), 135 (31), 91 (59), 69 (37), 57 (36), and 55 (100).

Anal. Calcd for $C_{26}H_{34}O_5Si$ (454.64): C, 68.69; H, 7.54. Found: C, 68.58; H, 7.62.

1,5-Di-*O*-acetyl-2,3-*O*-cyclopentylidene-β-D-ribofuranose (6). To a solution of **2** (3.1 g, 14.3 mmol) in dry pyridine (20 mL), acetic anhydride (3 mL) was added. After 12 h at room temperature and removal of pyridine by distillation, the residual syrup was dissolved in ethyl acetate (50 mL), washed with a saturated $NaHCO_3$ solution (10 mL), then with water (2x10 mL), and finally purified by column chromatography on silica gel (AcOEt/hexane 1:4) to give 2.25 g (52%) of **6**, bp 153 °C, 0.03 Torr, $[\alpha]_D^{22}$ -27.5° (*c* 1.2); λ_{max}^{EtOH} 210 nm (ε 110); ν_{max}^{KBr} 1748, 1280, 1110, and 970 cm^{-1}. ^1H NMR (200 MHz,

$CDCl_3$): δ 6.20 (*s*, 1 H, H-1), 4.63 (*broad s*, 2 H, H-2 and H-3), 4.46 (*t*, 1 H, $J_{4,5a}$ 7 Hz, $J_{4,5b}$ 11 Hz, H-4), 4.12 (*dd*, $J_{5a,5b}$ 7.5 Hz, Hb-5), 4.08 (*dd*, 1 H, Ha-5), 2.08 and 2.03 (*2 s*, 2x3 H, 2 Ac), 2.13 and 1.55 (*2 m*, 8 H, cyclopent.). MS: *m/z* 300(4, M^+), 271 (16), 241 (15), 157 (12), 151 (22), 139 (100), 97 (86), 85 (41), 57 (21), 56 (26), and 55 (95).

Anal. Calcd for $C_{14}H_{20}O_7$ (300.31): C, 55.99; H, 6.71. Found: C, 55.72; H, 6.60.

1,5-Di-*O*-benzoyl-2,3-*O*-cyclopentylidene-β-D-ribofuranose (7). To a solution of 2 (216 mg, 1 mmol) in pyridine (50 mL), benzoyl chloride (282 mg, 2 mmol) was added. After 12 h at room temperature the reaction mixture was treated as usual to give after column chromatography on silica gel (AcOEt/hexane 1:2) 350 mg (83%) of 7, mp 98.6-103.6 °C, $[\alpha]_D^{23}$ - 51.8°(*c* 1.7); λ_{max}^{EtOH} 202 (ε 20690), and 230 nm (24410); ν_{max}^{KBr} 1715, 1270, 1110, 1100,1025, and 965 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 8.12-7.35 (*m*, 10 H, 2 Bz.), 6.55 (*s*, 1 H, H-1), 4.94 (*d*, 1 H, $J_{2,3}$ 5.8 Hz, H-2), 4.90 (*broad d*, 1 H, $J_{3,4}$ 0.5 Hz, H-3), 4.73 (*broad t*, 1 H, $J_{4,5a}$ 6 Hz, $J_{4,5b}$ 6 Hz, H-4), 4.50 (*dd*, 1 H, $J_{5a,5b}$ 9.4 Hz, Hb-5), 4.44 (*dd*, 1 H, Ha-5), 2.03 and 1.78 (*2 m*, 8 H, cyclopent.). MS: *m/z* 201 (17), 106 (9), 105 (100), 81 (5), 77 (25), 55 (15), and 51 (6).

Anal. Calcd for $C_{24}H_{24}O_7$ (424.45): C, 67.91; H, 5.70. Found: C, 67.79; H, 5.73.

1,5-Di-*O*-(*tert*-butyldimethylsilyl)-2,3-*O*-cyclopentylidene-α- and β-D-ribofuranoses (8). Syrup, $[\alpha]_D^{27}$ -9.9° (*c* 0.9); λ_{max}^{EtOH} 228 nm (ε 180); ν_{max}^{KBr} 1465, 1330, 1255, 1160, and 1110 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): α isomer δ 5.41 (*d*, 1 H, $J_{1,2}$ 4 Hz, H-1), 4.57 (*dd*, 1 H, $J_{2,3}$ 7 Hz, $J_{3,4}$ 2.2 Hz, H-3), 4.50 (*dd*, 1 H, H-2), 4.20 (*ddd*, 1 H, $J_{4,5a}$ 3 Hz, $J_{4,5b}$ 3 Hz, H-4), 3.74 (*dd*, 1 H, $J_{5a,5b}$ 11 Hz, Hb-5), 3.69 (*dd*, 1 H, Ha-5), 1.91 and 1.69 (*2 m*, 8 H, cyclopent.), 0.94 and 0.90 (*2 s*, 2x9 H, 2 Me_3C), 0.16 and 0.10 (*2 s*, 4x3 H, 4 MeSi); β isomer δ 5.38 (*s*, 1 H, H-1)), 4.70 (*d*, 1 H, $J_{2,3}$ 6 Hz, $J_{3,4}$ 1 Hz, H-3), 4.49 (*d*, 1 H, H-2), 4.20 (*m*, 1 H, $J_{4,5a}$ 9.5 Hz, $J_{4,5b}$ 6 Hz, H-C4), 3.65 (*dd*, 1 H, $J_{5a,5b}$ 11 Hz, Hb-5), 3.58 (*dd*, 1 H, Ha-5), 1.91 and 1.69 (*2 m*, 8 H, cyclopent.), 0.93 and 0.90 (*2s*, 2x9 H, 2 Me_3C), 0.15 and 0.12 (*2s*, 4x3 H, 4 MeSi). MS: *m/z* 387 (14), 303 (14), 273 (8), 171 (14), 143 (40), 117 (19), and 73 (100).

Anal. Calcd for $C_{22}H_{44}O_5Si_2$ (444.76): C, 59.41; H, 9.97. Found: C, 59.31; H, 10.01.

1,5-Di-*O*-(-*tert*-butyldiphenylsilyl)-2,3-*O*-cyclopentylidene-α- and β-D-ribofuranoses (9). Syrup, $[\alpha]_D^{22}$ -14.6° (*c* 1.4); λ_{max}^{EtOH} 207 (ε 27180), 220 nm (24110); ν_{max}^{KBr}

1470, 1335, 1110, and 980 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): α isomer δ 7.90-7.25 (*m*, 20 H, Ar), 5.49 (*d*, 1 H, $J_{1,2}$ 4 Hz, H-1), 4.66 (*dd*, 1 H, $J_{2,3}$ 6.5 Hz, $J_{3,4}$ 2, H-3), 4.58 (*dd*, 1 H, H-2), 4.30 (*m*, 1 H, H-4), 3.70 (*m*, 2 H, 2H-5), 1.90 and 1.70 (*2 m*, 8 H, cyclopent.), 1.05 (*m*, 18 H, 2 Me_3C); β isomer δ 7.90-7.25 (*m*, 20 H, Ar), 5.25(*s*, 1 H, H-1), 4.66 (*m*, 1 H, H-3), 4.60 (*m*, 1 H, H-2), 4.26 (*m*, 1 H, H-4), 3.70 (*m*, 2 H, 2H-5), 1.90 and 1.70 (*2 m*, 8 H, cyclopent.), and 1.05 (*m*, 18 H, 2 Me_3C). MS: *m/z* 635 (10), 551 (7), 473 (14), 199 (63), 135 (100), and 91 (20).

Anal. Calcd for $C_{42}H_{52}O_5Si_2$ (693.05): C, 72.79; H, 7.56. Found: C, 72.67; H, 7.47.

1,5-Anhydro-2,3-*O*-cyclopentylidene-β-D-ribofuranose (10). Obtained as described for the preparation of **2**, bp 70 °C, 0.1 Torr, $[\alpha]_D^{28}$ -62.0° (*c* 1.3); λ_{max}^{EtOH} 228 nm (ε 52); ν_{max}^{KBr} 1335, 1210, 1110, and 1060 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 5.48 (*s*, 1 H, H-1), 4.76 (*d*, 1 H, $J_{3,4}$ 0 Hz, $J_{4,5a}$ 0 Hz, $J_{4,5b}$ 3.8 Hz, H-4), 4.30-4.26 (*m*, 2 H, H-2 and H-3), 3.45 (*dd*, 1 H, $J_{5a,5b}$ 7.2 Hz, Hb-5), 3.31 (*d*, 1 H, Ha-5), 1.93 and 1.67 (*2 m*, 8 H, cyclopent.). MS: *m/z* 198 (3,M^+), 169 (68), 114 (8), 97 (9), 84 (78), 68 (44), and 55 (100).

Anal. Calcd for $C_{10}H_{14}O_4$ (198.22): C, 60.59; H, 7.12. Found: C, 60.54; H, 7.02.

1,2:3,5-Di-*O*-cyclopentylidene-α-D-xylofuranose (12). A mixture of D-xylose (5g, 30 mmol), cupric sulfate (5g, 30 mmol) and concentrated sulfuric acid (1 mL) in dry cyclopentanone (150 mL) was kept at room temperature under vigorous stirring for 36 h, then neutralized by addition of $NaHCO_3$ (5g, 0.06 mmol). After 2 h the cyclopentanone was distilled and the residue extracted with ether (100 mL). The organic phase was washed with water (2x50 mL), dried (Na_2SO_4) and concentrated to give 4.5 g (53%) of crude **12**. The analytically pure sample was obtained by crystallization in ethanol, mp 88.4-89.1 °C. $[\alpha]_D^{18}$ +11.1° (*c* 1.2); λ_{max}^{EtOH} 202 nm (ε 100); ν_{max}^{KBr} 1340, 1200, 1135, 1100, 1000, and 980 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 6.00 (*d*, 1 H, $J_{1,2}$ 4 Hz, H-1), 4.45 (*d*, 1 H, H-2), 4.25 (*d*, 1 H, $J_{3,4}$ 2 Hz, H-3), 4.20 (*dd*, 1 H, $J_{4,5b}$ 1.5 Hz, $J_{5a,5b}$ 14 Hz, Hb-5), 4.05 (*dd*, 1 H, $J_{4,5a}$ 2 Hz, Ha-5), 4.02 (*m*, 1 H, H-4), 1.89 and 1.72 (*2 m*, 2x8 H, 2 cyclopent.). MS: *m/z* 282 (18, M^+), 253 (93), 169 (47), 139 (17), 97 (28), 85 (34), 69 (31), and 55 (100).

Anal. Calcd for $C_{15}H_{22}O_5$ (282.34): C, 63.81; H, 7.85. Found: C, 63.67; H, 7.91.

1,2-*O*-Cyclopentylidene-α-D-xylofuranose (13). A solution of **12** (2.82g, 0.01 mmol) in a mixture of methanol (150 mL) and HCl 1M (50 mL), was kept at room temperature until the reaction was completed (TLC, 2-3h), then immediately neutralized by addi-

tion of $NaHCO_3$ (3 g, 0.035 mmol) in order to avoid further cleavage of the 1,2-*O*-cyclopentylidene group. The mixture was stirred for 30 min then concentrated to dryness and the residue extracted with hot ethyl acetate (3x50 mL). Concentration of the combined organic layers left a white solid which, after crystallization in heptane gave **13** (1.5 g, 69%), mp 73.8-74.2 °C, $[\alpha]_D^{18}$-4.2° (*c* 1.2); λ_{max}^{EtOH} 202 (ε 30), and 220 nm (20); ν_{max}^{KBr} 3500, 1345, 1205, 1115, 1050, and 1020 cm^{-1}. ^1H NMR (200 MHz, CD_3OD): δ5.89 (*d*, 1 H, $J_{1,2}$ 4 Hz, H-1), 4.40 (*d*, 1 H, H-2), 4.18 (*ddd*, 1 H, $J_{3,4}$ 3 Hz, $J_{4,5a}$ 5 Hz, $J_{4,5b}$ 6 Hz, H-4), 4.15 (*d*, 1 H, H-3), 3.80 (*dd*, 1 H, $J_{5a,5b}$ 11 Hz, Hb-5), 3.76 (*dd*, 1 H, Ha-5), 1.90 and 1.67 (*2 m*, 8 H, cyclopent.). MS: *m/z* 216 (9, M^+), 187 (75),139 (61), 123 (9), 97 (10), 85 (66), 67 (25), and 55 (100).

Anal. Calcd for $C_{10}H_{16}O_5$ (216.24): C, 55.55; H, 7.46. Found: C, 55.53; H, 7.37.

1,2-*O*-Cyclopentylidene-5-*O*-toluyl-α-D-xylofuranose (14). To a solution of **13** (500 mg, 2.3 mmol) in dry pyridine (50 mL), p-toluyl chloride (0.33 mL, 2.5 mmol) was added. After 40 min stirring at room temperature, a classical treatment gave after column chromatography on silica gel (AcOEt/hexane 1:2) 690 mg (89%) of **14** which was recrystallized in hexane, mp 114.3-115.7 °C, $[\alpha]_D^{23}$ +16.7° (*c* 0.9), λ_{max}^{EtOH} 203 (ε 20120), and 239 nm (14290); ν_{max}^{KBr} 3450, and 1740 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 7.95 and 7.26 (*AA'BB' system*, 4 H, Tol.), 5.93 (*d*, 1H, $J_{1,2}$ 4 Hz, H-1), 4.77 (*dd*, 1 H, $J_{4,5b}$ 8 Hz, $J_{5a,5b}$ 12 Hz, Hb-5), 4.54 (*d*, 1 H, H-2), 4.36 (*ddd*, 1 H, $J_{3,4}$ 2 Hz, $J_{4,5a}$ 4.7 Hz, H-4), 4.34 (*dd*, 1 H, Ha-5), 4.16 (*dd*, 1 H, $J_{3,OH}$ 3.5 Hz, H-3), 3.38 (*d*, 1 H, OH), 2.42 (*s*, 3 H, CH_3-Ar), 2.10 and 1.55 (*2 m*, 8 H, cyclopent.). MS: *m/z* 334 (1, M^+), 305 (2), 221 (5), 136 (5), 119 (100), 97 (7), 91 (21), 85 (17), 65 (9), and 55 (32).

Anal. Calcd for $C_{18}H_{22}O_6$ (334.37): C, 64.66; H, 6.63. Found: C, 64.63; H, 6.59.

1,2-*O*-Cyclopentylidene-5-*O*-trityl-α-D-xylofuranose (15). To a solution of **13** (1 g, 4.6 mmol) in dry pyridine (50 mL), trityl chloride (1.42 g, 5.1 mmol) was added. After 60 h at room temperature and concentration to dryness, the residue submitted to column chromatography on silica gel (AcOEt/hexane 1:3) gave 657 mg (31%) of **15** which was recrystallized in hexane, mp 130.5-132.2 °C $[\alpha]_D^{25}$ +12.6° (*c* 0.8); λ_{max}^{EtOH} 203 nm (ε 53700) ; ν_{max}^{KBr} 3510 cm^{-1}. ^1H NMR (200 MHz, C_6D_6): δ 6.95-7.70 (*m*, 15 H, Ar), 6.00 (*d*, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 4.41 (*ddd*, 1 H, $J_{3,4}$ 4.6 Hz, $J_{4,5a}$ 4.5 Hz, $J_{4,5b}$ 5 Hz, H-4)), 4.36 (*d*, 1 H,

H-2), 4.19 (*broad d*, 1 H, $J_{3,OH}$ 1.4 Hz, H-3), 3.64 (*dd*, 1 H, $J_{5a,5b}$ 10 Hz, Hb-5), 3.55 (*dd*, 1 H, Ha-5), 2.75 (*broad s*, 1 H, OH), 2.00 and 1.55 (*2 m*, 8 H, cyclopent.). MS: *m/z* 458 (2), 381 (11), 259 (20), 243 (100), 185 (55), 165 (92), 115 (32), 85 (69), 77 (64), and 67 (57).

Anal. Calcd for $C_{29}H_{30}O_5$ (458.56): C, 75.96; H, 6.59. Found: C, 75.81; H, 6.55.

5-*O*-*tert*-Butyldiphenylsilyl-1,2-*O*-cyclopentylidene-α-D-xylofuranose (16). To a solution of **13** (3g, 13.9 mmol) in dry CH_2Cl_2 (20 mL), *tert*-butyldiphenylchlorosilane (5.32 mL, 20.8 mmol), triethylamine (2.88 mL, 20.8 mmol) and *N,N*-dimethylaminopyridine (0.17 g, 1.4 mmol) were added. The mixture was allowed to react at room temperature for 90 min, then concentrated to dryness. The obtained syrup was extracted with ether (50 mL), and the organic phase washed with water (2x10 mL), dried (Na_2SO_4) and concentrated gave after column chromatography on silica gel (AcOEt/hexane 1:5) 3.4 g (54%) of **16**, which was crystallized in a mixture of ether and hexane, mp 76.1-77.0 °C, $[\alpha]_D^{21}$ -8.7° (*c* 1.1); λ_{max}^{EtOH} 205 (ε 45430), 218 (36430), and 259 nm (2110); ν_{max}^{KBr} 3430 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 7.35- 7.80 (*m*, 10 H, Ar), 6.01 (*d*, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 4.52 (*d*, 1 H, H-2), 4.43 (*dd*, 1 H, $J_{3,4}$ 2 Hz, $J_{3,OH}$ 3.2 Hz, H-3), 4.18 (*m*, 1 H, $J_{4,5a} = J_{4,5b}$ 3.2 Hz, H-4), 4.14 (*broad d*, 2 H, 2 H-5), 4.12 (*d*, 1 H, OH), 2.11 and 1.65 (*2 m*, 8 H, cyclopent.), and 1.13 (*s*, 9 H, $(CH_3)_3C$). MS. *m/z* 397 (4, M^+), 313 (2), 295 (11), 283 (8), 235 (40), 199 (84), 163 (100), 135 (51), 91 (57), and 55 (72).

Anal. Calcd for $C_{26}H_{34}O_5Si$ (454.64): C, 68.69; H, 7.54. Found: C, 68.60; H, 7.54.

1,2-*O*-Cyclopentylidene-5-*O*-toluyl-α-D-ribofuranos-3-ulose (17). To a mixture of pyridine (60 mL) and CH_2Cl_2 (900 mL) was added CrO_3 (32.8 g, 328 mmol) and the suspension vigorously stirred for 30 min. A solution of **14** (9.11 g, 27.25 mmol) in CH_2Cl_2 was added and the mixture allowed to react at room temperature for 45 min then cooled (4 °C) and neutralized with a saturated $NaHCO_3$ solution (300 mL). The organic layer was separated, dried (Na_2SO_4) and concentrated. The brown residue was extracted with ether (200 mL), filtered and treated with active charcoal (2g) for 15 min. After filtration and concentration, the obtained yellowish syrup purified by column chromatography on silica gel (Et_2O) gave 5.98 g (66%) of **17**, mp 131.5-131.9 °C, $[\alpha]_D^{21}$ +127.7° (*c* 1.0); λ_{max}^{EtOH} 203 (ε 21670), and 240 nm (13130); ν_{max}^{KBr} 1775 and 1725 cm^{-1}. ^1H NMR (200 MHz, C_6D_6): δ 7.87 and 6.78 (*AA'BB' system*, 4 H, Ar), 5.65 (*d*, 1 H, $J_{1,2}$ 4.5 Hz, H-1), 4.48 (*dd*, 1 H, $J_{4,5b}$ 4 Hz, $J_{5a,5b}$ 13 Hz, Hb-5), 4.17 (*dd*,

1 H, $J_{4,5a}$ 3.5 Hz, Ha-5), 4.13 (*broad dd*, 1 H, $J_{2,4}$ 1 Hz, H-4), 3.93 (*broad d*, 1 H, H-2), 1.94 (*s*, 3 H, CH_3-Ar), 1.90 and 1.32 (*2 m*, 8 H, cyclopent.). MS: *m/z* 167 (20), 126 (34), 119 (100), 97 (37), 91 (31), 65 (13), and 55 (44).

Anal. Calcd for $C_{18}H_{20}O_6$ (332.36): C, 65.05; H, 6.07. Found: C, 64.95; H, 6.20.

1,2-*O*-Cyclopentylidene-5-*O*-trityl-α-D-ribofuranos-3-ulose (18). Prepared as described for **17** from **15** (4.83 g, 10.53 mmol) gave **18** (4.11 g, 86%), mp 141.9-144.4 °C, $[\alpha]_D^{23}$ +103.3°(*c* 1.2); λ_{max}^{EtOH} 205 nm (ε 38210); ν_{max}^{KBr} 1770 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 7.10-7.80 (*m*, 15 H, Ar), 6.33 (*d*, 1 H, $J_{1,2}$ 5 Hz, H-1), 4.57 (*dd*, 1 H, $J_{2,4}$ 1 Hz, H-2), 4.37 (*ddd*, 1 H, $J_{4,5a}$ 2.5 Hz, $J_{4,5b}$ 2.8 Hz, H-4), 3.52 (*dd*, 1 H, $J_{5a,5b}$ 10 Hz, Hb-5), 3.30 (*dd*, 1 H, Ha-5), 1.97 and 1.72 (*2 m*, 8 H, cyclopent.). MS: *m/z* 379 (6), 259 (9), 243 (100), 228 (14), 215 (11), 202 (7), 183 (27), 165 (99), and 126 (51).

Anal. Calcd for $C_{29}H_{28}O_5$ (456.54): C, 76.30; H, 6.18. Found: C, 76.00; H, 6.15.

5-*O*-*tert*-Butyldiphenylsilyl-1,2-*O*-cyclopentylidene-α-D-ribofuranos-3-ulose (19). Prepared from **16** (2.5 g, 5.5 mmol) as described for **17** gave **19** (1.21 g, 49%), syrup, $[\alpha]_D^{22}$ +103.8° (*c* 1.1); λ_{max}^{EtOH} 202 (ε 22970), and 219 nm (16380); ν_{max}^{KBr} 1775 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 7.22-7.82 (*m*, 10 H, Ar), 6.22 (*d*, 1 H, $J_{1,2}$ 4.5 Hz, H-1), 4.39 (*broad d*, 1 H, $J_{2,4}$ 0.3 Hz, H-2), 4.32 (*m*, 1 H, $J_{4,5a}$ 1.5 Hz, $J_{4,5b}$ 2 Hz, H-4), 3.90 (*dd*, 1 H, $J_{5a,5b}$ 11 Hz, Ha-5), 3.80 (*dd*, 1 H, Hb-5), 2.07 and 1.53 (*2 m*, 8 H, cyclopent.), and 0.97(*s*, 9 H, $(CH_3)_3C$). MS: *m/z* 395 (11), 311 (9), 283 (24), 241 (63), 223 (25), 199 (51), 163 (100), 115 (38), 105 (32), and 97 (36).

Anal. Calcd for $C_{26}H_{32}O_5Si$ (452.62): C, 68.99; H, 7.13. Found: C, 68.79; H, 7.23.

1,2-*O*-Cyclopentylidene-5-*O*-toluyl-α-D-ribofuranose (20). To a solution of **17** (1g, 3 mmol) in 1:1 MeOH/H_2O (100 mL), $NaBH_4$ (0.34 g, 9 mmol) was added portion-wise and allowed to react at room temperature for 12 h. After concentration and extraction with ether (50 mL), the organic layer was separated, dried (Na_2SO_4) and submitted to column chromatography on silica gel (AcOEt/hexane 1:3) to give **20** (0.6 g,60%), mp 100.5 - 103.0 °C, $[\alpha]_D^{21}$ +29.7° (*c* 1.5); λ_{max}^{EtOH} 204 (ε 15900), and 239 nm (15300); ν_{max}^{KBr} 3450 and 1730 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 8.33 and 7.43 (*AA'BB' system*, 4 H, Ar), 6.08 (*d*, 1 H, $J_{1,2}$ 4 Hz, H-1), 4.95 (*dd*, 1 H, $J_{4,5b}$ 2.5 Hz, $J_{5a,5b}$ 12.4 Hz, Hb-5), 4.78 (*dd*, 1 H, $J_{2,3}$ 5.2 Hz, H-2), 4.68 (*dd*, 1 H, $J_{4,5a}$ 5 Hz, Ha-5), 4.33 (*ddd*, 1 H, $J_{3,4}$ 9 Hz, H-4), 4.18 (*ddd*, 1 H, $J_{3,OH}$ 10.3 Hz, H-3), 2.83 (*d*, 1 H,

OH), 2.68 (*s*, 3 H, CH_3-Ar), 2.33 and 1.73 (*2 m*, 8 H, cyclopent.). MS: *m/z* 334 (2, M^+), 305 (5), 151 (8), 136 (8), 119 (100), 91 (24), 85 (23), and 55 (41).

Anal. Calcd for $C_{18}H_{22}O_6$ (334.37): C, 64.66; H, 6.63. Found: C, 64.40; H, 6.55.

1,2-*O*-Cyclopentylidene-5-*O*-trityl-α-D-ribofuranose (21). Prepared from **18** (1.5 g, 3.3 mmol) as described for **20** gave **21** (1.11 g, 74%), mp 75.9 - 78.1 °C, $[\alpha]_D^{26}$ +29.0° (*c* 1.1); λ_{max}^{EtOH} 204 nm (ε 43780); ν_{max}^{KBr} 3470 cm^{-1}. ^1H NMR (200 MHz, C_6D_6): δ 6.95 - 7.74 (*m*, 15 H, Ar), 5.58 (*d*, 1 H, $J_{1,2}$ 4 Hz, H-1), 4.00 (*ddd*, 1 H, $J_{3,4}$ 8.8 Hz, $J_{4,5a}$ 5 Hz, $J_{4,5b}$ 2.5 Hz, H-4), 3.99 (*dd*, 1 H, $J_{2,3}$ 5 Hz, H-2), 3.81 (*ddd*, 1 H, $J_{3,OH}$ 10 Hz, H-3), 3.58 (*dd*, 1 H, $J_{5a,5b}$ 10 Hz, Hb-5), 3.39 (*dd*, 1 H, Ha-5), 2.08 (*d*, 1 H, OH), 2.01 and 1.65 (*2 m*, 8 H, cyclopent.). MS: *m/z* 381 (4), 374 (4), 259 (5), 243 (100), 185 (18), 165 (84), 105 (53), 85 (57), and 55 (85).

Anal. Calcd for $C_{29}H_{30}O_5$ (458.56): C, 75.96; H, 6.59. Found: C, 75.74; H, 6.64.

5-O-*tert*-Butyldiphenylsilyl-1,2-*O*-cyclopentylidene-α-D-ribofuranose (22). Prepared from **19** (4.1 g, 9.04 mmol) as described for **20**, gave **22** (2.5 g, 60%), mp 77.4-79.4 °C, $[\alpha]_D^{28}$ +31.1° (*c* 1.0); λ_{max}^{EtOH} 204 (ε 27400), and 220 nm (28350); ν_{max}^{KBr} 3550 cm^{-1}. ^1H NMR (200 MHz, $(CD_3)_2CO$): δ 7.25-7.73 (*m*, 10 H, Ar), 5.70 (*d*, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 4.47 (*dd*, 1 H, $J_{2,3}$ 4.2 Hz, H-2), 3.99 (*dt*, 1 H, $J_{3,4}$ 9 Hz, $J_{3,OH}$ 9 Hz, H-3), 3.92 (*ddd*, 1 H, $J_{4,5a}$ 4 Hz, $J_{4,5b}$ 1.5 Hz, H-4), 3.90 (*dd*, 1 H, $J_{5a,5b}$ 10.5 Hz, Hb-5), 3.85 (*d*, 1 H, OH), 3.75 (*dd*, 1 H, Ha-5), 1.84 and 1.60 (*2 m*, 8 H, cyclopent.), and 0.94 (*s*, 9 H, $(CH_3)_3C$). MS: *m/z* 397 (2), 313 (5), 295 (5), 283 (6), 199 (53), 163 (79), 135 (33), 91 (48), 57 (38), and 55 (100).

Anal. Calcd for $C_{26}H_{34}O_5Si$ (454.64): C, 68.69; H, 7.54. Found: C, 68.64; H, 7.57.

Recycling of the cyclopentanone

The unreacted cyclopentanone was separated and stored for a few days over dry K_2CO_3, then directly distilled. Almost 80% of pure cyclopentanone (bp 130 °C), suitable for reuse was recovered.

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