SYNTHESIS OF 3,4-DI-O-BENZYL-1,2-O-(1-CYANO) ETHYLIDENE-α-D-XYLOPYRANOSE

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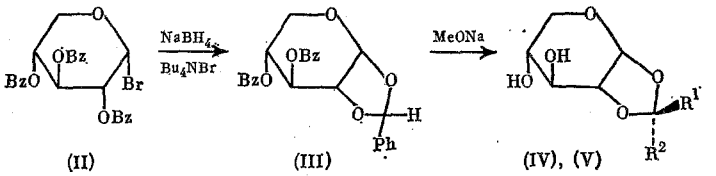
The acylated 1,2-O-cyanoalkylidene derivatives of D-xylopyranose are used successfully for the stereospecific glycosylation of a number of trityl ethers of monosaccharides [1]. To study the effect of the type of protective groups on the stereospecificity of the glycosylation of the trityl ethers of monosaccharides by the 1,2-O-cyanoethylidene derivatives of D-xylopyranose it was necessary for us to obtain 3,4-di-O-benzyl-1,2-O-(1-cyano)ethylidene-α-D-xylopyranose (I).

We synthesized (I) by the following scheme. The reaction of 2,3,4-tri-O-benzoyl-α-D-xylopyranosyl bromide (II) [2] with $NaBH_4$ in MeCN in the presence of Bu_4NBr, i.e., under the conditions of the general method for the synthesis of the 1,2-O-benzylidene derivatives of neutral sugars [3], gave 3,4-di-O-benzoyl-1,2-O-benzylidene-α-D-xylopyranose (III), which was then converted by Zemplen debenzoylation to a mixture of the exo- and endo-phenyl derivatives (IV) and (V) in a 1:5.7 ratio (based on the PMR spectral data for the reaction mixture). The pure (IV) and (V) were isolated by column chromatography.

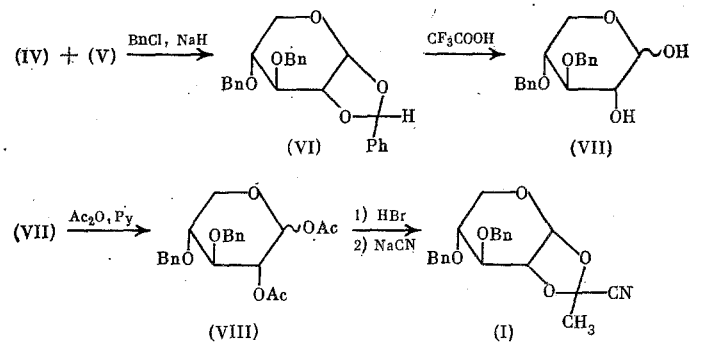


(II) (III) (IV), (V)

R^1 = Ph, R^2 = H(IV); R^1 = H, R^2 = Ph(V).

The structure of the 1,2-O-benzylidene derivatives (IV) and (V) was confirmed by the data of the PMR spectra, which, besides the other signals, had singlets at 6.19 and 5.82 ppm, which belong to the endo and exo protons at the C^2 atom of the dioxolane ring.

Benzylation of the (IV) + (V) mixture gave 3,4-di-O-benzyl-1,2-O-benzylidene-α-D-xylopyranose (VI), the deacetalation of which with aqueous CF_3COOH solution gave 3,4-di-O-benzyl-D-xylopyranose (VII). 1,2-Di-O-acetyl-3,4-di-O-benzyl-D-xylopyranose (VIII) was synthesized by the acetylation of diol (VII). The treatment of the di-O-acetyl derivative (VIII) with a $CHCl_3$ solution of HBr gave 2-O-acetyl-3,4-di-O-benzyl-D-xylopyranosyl bromide, which by treatment with NaCN under the conditions described in [4] was converted to a mixture of the exo- and endo-cyano isomers (I). The pure (I) isomers were not isolated due to their close chromatographic mobilities.



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The structure of (I) was confirmed by the elemental analysis and the PMR and ^{13}C NMR spectral data. The PMR spectrum had two singlets at δ 1.82 and 1.74 ppm (the ratio of their integral intensities was ~ 4:1) and the endo and exo CCH_3 groups at the C^2 atom of the dioxolane ring. The ^{13}C NMR spectrum had signals at δ 24.9, 27.2, 99.05, 99.1, 117.1, 117.9 ppm, which belong to the $C\underline{C}H_3$, $C\underline{C}H_3$, and CN atoms in the exo- and endocyano isomers (I).

EXPERIMENTAL

The melting points were determined on a Kofler stand. The optical rotations were measured in $CHCl_3$ solution on a Perkin-Elmer 141 polarimeter at 20 ±2°C. The NMR spectra were taken in $CDCl_3$ solution using TMS as the internal standard. The PMR spectra were obtained on Varian DA-60-IL (60 MHz), Tesla BS-497 (100 MHz), and Bruker WM-250 (250 MHz) instruments. To simplify the PMR spectra of diols (IV) and (V) their $CDCl_3$ solutions were shaken with D_2O in the PMR spectrometer ampuls and the spectrum was recorded after complete stratification of the formed mixture. The ^{13}C NMR spectrum was obtained on a Bruker WM-250 instrument at a ^{13}C operating frequency of 62.89 MHz. The MeCN was distilled over P_2O_5 and then over CaH_2. The DMF was dried over KOH and then distilled over CaH_2. The analytical grade NaCN (Czechoslovakia) was ground, and dried for 10 h over P_2O_5 in vacuo at 100°. The cp Bu_4NBr was recrystallized from ethyl acetate. The TLC was run on plates covered with silica gel L5/40 μm (Czechoslovakia), and the substances were detected using 25% H_2SO_4 solution and subsequent heating at ~ 150°. The solvent systems for the TLC were: A) 1:1 ether–benzene; B) 1:2 ether–benzene; C) 93:7 chloroform–methanol. The column chromatography was run on silica gel L40/100 μm (Czechoslovakia), using gradient elution from benzene to ether (D) and from chloroform to ethanol (E).

1,2-O-(S- and R-Benzylidene)-α-D-xylopyranose (IV) and (V). With stirring, 2.92 g (5.58 mmoles) of (II) [2] and 0.91 g (2.8 mmoles) of Bu_4NBr were dissolved (20°, ~ 1 h) in 10 ml of MeCN. To the obtained solution was added 0.32 g (8.4 mmoles) of $NaBH_4$ and the mixture was stirred for 1 h, cooled with tap water, and then stirred again for 16 h at 20°. The mixture was concentrated, diluted with 100 ml of $CHCl_3$, washed with water (4 × 40 ml), and evaporated. The residue was deposited on an Al_2O_3 bed (~ 3 cm), rinsed with 150 ml of a 1:2 $CHCl_3$–petroleum ether mixture, concentrated, and the residue was dried in vacuo. The obtained dibenzoate (III) was dissolved in 10 ml of 0.1 M MeONa in abs. MeOH, let stand for 16 h, evaporated, and after column chromatography in system (E) we obtained 0.75 g of (V) and 0.58 g of a mixture of (IV) and (V), the recrystallization of which from an ethyl acetate–hexane mixture gave 100 mg of (IV). The total yield of (IV) and (V) was quantitative; mp 138-140°, $[\alpha]_D$ + 15.6° (C1) R_f 0.37 (C). PMR spectrum (δ ppm): 3.45-3.65 m (2H, H^4 and H^5), 3.73 d.d (1H, $H^{5'}$, $J_{4,5'} = 3.8$, $J_{5,5'} = 11.0$ Hz), 3.81 t (1H, H^3, J ~ 5 Hz), 4.09 t (1H, H^2, J ~ 5 Hz), 5.55 d (1H, H^1, $J_{1,2} = 4.1$ Hz), 6.19 s (1H, $PhC\underline{H}$), 7.3-7.6 m (5H, C_6H_5). Compound (V) is a colorless syrup, $[\alpha]_D$ + 20.0° (C3), R_f 0.28 (C). PMR spectrum (δ, ppm): 3.49 m (1H, H^4), 3.67 d.d (1H, H^5, $J_{4,5} = 5.1$, $J_{5,5'} = 11.8$ Hz), 3.82 d.d (1H, $H^{5'}$, $J_{4,5'} = 2.7$, $J_{5,5'} = 11.8$ Hz), 3.87t (H^3, J ~ 4 Hz), 3.99 t (1H, H^2, J ≃ 4 Hz), 5.39 d (1H, H^1, $J_{1,2} = 3.4$ Hz), 5.82s (1H, $PhC\underline{H}$), 7.3-7.6 m (5H, C_6H_5). Found for (IV): C 60.17; H 5.96%; for (V): C 60.44; H 5.88%. $C_{12}H_{14}O_5$. Calculated: C 60.50; H 5.92%.

3,4-Di-O-benzyl-D-xylopyranose (VII). With stirring, to a solution of 0.69 g (2.9 mmoles) of a mixture of (IV) and (V) in 5 ml of DMF at 0° was added 430 mg (9 mmoles) of a 50% suspension of NaH in oil, the mixture was stirred for 20 min, 1.1 ml (9 mmoles) of $PhCH_2Cl$ was added, the mixture was stirred for 2 h, diluted with 0.5 ml of MeOH, and the mixture was concentrated, diluted with 75 ml of $CHCl_3$, and washed with water (3 × 25 ml). The organic layer was separated, concentrated, and dibenzyl ether (VI) was isolated from the residue by column chromatography. The obtained (VI) was dissolved in 18 ml of $CHCl_3$, 2 ml of 90% CF_3COOH was added, and the mixture was let stand for 1 h. At the end of reaction (checked by TLC) the mixture was evaporated, coevaporated with toluene (2 × 25 ml), and the residue was recrystallized from a $CHCl_3$–hexane mixture to give 1.01 g (84% yield) of diol (VII), mp 135-139°, $[\alpha]_D$ −14.0° (C 0.5), R_f 0.15 (A). PMR spectrum (δ, ppm): 3.45-4.18 m (7H, H^2, H^3, H^4, $H^{5'}$; 2OH), 4.53-4.78 m (4H, $2C\underline{H}_2Ph$), 4.82 d (0.3H, H_β^1, $J_{1,2} = 4.2$ Hz), 4.95 d (0.7H, H_α^1, $J_{1,2} = 1.9$ Hz), 7.27-7.35 m (10H, $2C_6H_5$). Found: C 68.85; H 6.76%. $C_{19}H_{22}O_5$. Calculated: C 69.07; H 6.71%.

1,2-Di-O-acetyl-3,4-di-O-benzyl-D-xylopyranose (VIII). A solution of 0.90 g (2.7 mmoles) of diol (VII) in a mixture of 2 ml of pyridine and 1 ml of Ac_2O was let stand for 16 h, 0.5 ml of MeOH was added, and the mixture was let stand for 10 min. The reaction mixture was diluted with 50 ml of $CHCl_3$, washed with water (2 × 25 ml), the organic layer was separated, concentrated, and subjected to column chromatography (system D) and the residue gave 1.04 g (93%) of diacetate (VIII) as a colorless syrup, $[\alpha]_D$ + 60.1° (C 2), R_f 0.53 (B). PMR spectrum (δ, ppm): 3.53-3.98 m (4H, H^3, H^4, $H^{5'}$), 4.46-5.04 m (5H, H^2, $2C\underline{H}_2Ph$), 5.54 d (0.25 H, H_β^1, $J_{1,2} =$

7.5 Hz), 6.17 d (0.75H, $H_\alpha{}^1$, $J_{1,2}$ = 3.8 Hz), 7.15-7.37 m (10H, $2C_6H_5$). Found: C 66.36; H 6.30%. $C_{23}H_{26}O_7$. Calculated: C 66.65; H 6.32%.

3,4-Di-O-benzyl-1,2-O-(1-cyano)ethylidene-α-D-xylopyranose (I). To a solution of 1.4 g (3.4 mmoles) of diacetate (VIII) in 5 ml of $CHCl_3$ was added 10 ml of a 1 M HBr solution in $CHCl_3$, which was obtained by the slow addition at 0° of 0.4 ml (10 mmoles) of MeOH to a solution of 0.75 ml (10 mmoles) of AcBr in 9 ml of $CHCl_3$. After 20 min (checked by TLC, R_f of formed 2-O-acetyl-3,4-di-O-benzyl-D-xylopyranosyl bromide = 0.71 (B)) the reaction mixture was diluted with ~ 70 ml of $CHCl_3$, washed with ice water (3 × 25 ml), the organic layer was separated, evaporated, and the residue was dried in vacuo. The obtained substance was dissolved in 5 ml of MeCN, 0.55 g (1.7 mmoles) of Bu_4NBr was added, the mixture was stirred for 1 h, 0.83 g (17 mmoles) of NaCN was added, and the mixture was stirred for 16 h. The reaction mixture was concentrated, diluted with 200 ml of a 1:2 $CHCl_3$–hexane mixture, and washed with water (8 × 50 ml). The organic layer was separated, concentrated, dissolved in 3 ml of $CHCl_3$, deposited on an Al_2O_3 bed (~ 5 × 2 cm), and rinsed with 100 ml of a 1:2 $CHCl_3$–hexane mixture. The eluate was concentrated and column chromatography (system D) of the residue gave 0.92 g (71%) of acetal (I) as a colorless syrup, $[\alpha]_D$ + 25.2° (C 1), R_f 0.76 (B). PMR spectrum (δ, ppm): 1.75 s (0.6H, CCH_3 of endo-cyano isomer), 1.82 s (2, 4H, CCH_3 of exo-cyano isomer), 3.44-4.27 m (4H, H^3, H^4, H^5, $H^{5'}$), 4.30-4.76 m (5H, H^2, $2CH_2Ph$), 5.47 d (0.2H, H^1 of endo-cyano isomer, $J_{1,2}$ = 4.2 Hz), 5.61 d (0.8H, H^1 of exo-cyano isomer, $J_{1,2}$ = 4.8 Hz), 7.14-7.42 m (10H, $2C_6H_5$). Found: C 68.80; H 6.38; N 3.41%. $C_{22}H_{23}NO_5$. Calculated: C 69.27; H 6.08; N 3.69%.

CONCLUSIONS

The synthesis of 3,4-di-O-benzyl-1,2-O-(1-cyano)ethylidene-α-D-xylopyranose was described, using 1,2-O-benzylidene-α-D-xylopyranose as the key intermediate.

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^{13}C NMR OF (AROYLOXYMETHYL)TRIFLUOROSILANES

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Based on the x-ray structure analysis, IR spectroscopy, dielectrometry [1-3], and ^{19}F and ^{29}Si NMR [4] data, in the crystals and solutions of (aroyloxymethyl)trifluorosilanes $XC_6H_4COOCH_2SiF_3$ (I) the silicon atom is pentacoordinated due to intramolecular coordination with the oxygen atom of the C=O group. The degree of Si ← O interaction increases with increase in the π and σ electron-donor capacity of the X substituent.

For a more detailed study of the spectral characteristics of the (I) compounds we studied their ^{13}C NMR spectra, which were compared with the spectra of the isostructural tetracoordinated silicon derivatives, the (aroyloxymethyl)triethoxysilanes $XC_6H_4COOCH_2Si(OC_2H_5)_3$ (II), (X = 4-CH_3O and 4-NO_2), in which the intramolecular coordination bond is absent.

No difficulties are encountered in assigning the ^{13}C NMR lines of the aromatic fragments of the (I) and (II) molecules (Table 1). It was done taking into account the rule of the additive effect of substituents on the ^{13}C

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