SYNTHESIS OF THE PRINCIPAL CHAIN OF THE O-ANTIGENIC POLYSACCHARIDES OF *Shigella Flexneri*. COMMUNICATION 3.* SYNTHESIS OF 4-O-BENZOYL-3-O-(2-O-ACETYL-3,4-DI-O-BENZOYL-α-L-RHAMNOPYRANOSYL)-1,2-O-[1-(EXOCYANO)·ETHYLIDEN]-β-L-RHAMNOPYRANOSE

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We have previously reported the synthesis of 4-O-benzoyl-1,2-O-[1-(exocyano)ethyliden]-β-L-rhamnopyranose, 1,2-di-O-acetyl-3,4-di-O-benzoyl-L-rhamnopyranose, and methyl-3,4-di-O-benzoly-α-L-rhamnopyranoside, which are synthons A, B, and C for the construction of the tetrasaccharide monomer [1, 2].

We here report the synthesis of the disaccharide assembly BA (XI). Three approaches to the synthesis of this assembly have been developed, comprising glycosylation in the O^3 position of the rhamnose derivative containing the 1,2-O-cyanoethylidene group (compounds (II), (III), and (XVI)), together with, for comparison, (IV) and (V).

First of all, the diol (II) was chosen [3], obtained by reaction of the acetobromopyranose (XII) with NaCN in MeCN as described in [4] followed by deacetylation of the cyanoethylidene derivative (CED) (IIa). Treatment of the diacetate (IIa) with 0.01 M MeONa in a mixture of methanol and pyridine gave after purification by column chromatography (CC) the diol (II) in 94% yield.

Glycosylation of the diol (II) by treatment with 1 equiv. of the bromide (I) [2] in acetonitrile under Helferich conditions gave α-(1 → 3)- and α-(1 → 4)- disaccharides (VI) (40-45% yield) and (VII) (20% yield) together with the trisaccharide (VIII) (4% yield), 30% of the original diol (II) being recovered [5] (Scheme 1).

Increasing the amount of bromide (I) to 1.5 equiv. did not increase the yield of the required α-(1 → 3)-disaccharide (VI), but the yield of the trisaccharide (VIII) increased (10%) the yield of the α-(1 → 4)-disaccharide (VI) being 24%, and 10% of the starting diol (II) being recovered. The structures of the glycosylation products of the diol (II) were confirmed by acetylation and by their spectral data. The disaccharides (VI) and (VII) on acetylation with acetic anhydride in pyridine were converted into the isomeric diacetates (IX) and (X), respectively. The diacetate (IX) was identical with that obtained in high yield by glycosylation of 4-O-acetyl-1,2-O-[1-(exocyano)ethyliden]-β-L-rhamnopyranose (IV) [1, 6], and is therefore the (1 → 3)-bonded disaccharide. The trisaccharide (VIII) was not affected (TLC) by treatment with pyridine. Benzoylation of the (1 → 3)-disaccharide (VI) gave the tribenzoate (XI) with a single acetyl group at O^2 of the nonreducing rhamnose residue, i.e., the BA assembly. The structures of (VI)-(VIII) were confirmed by PMR spectral comparison with (IX)-(XI). The characteristic difference in the spectra of (IX) and (X) consists in the positions of the signals for H_A^3 and H_A^4. In the spectrum of the (1 → 3)- disacchardie (IX), a doublet of doublets for H_A^3 is seen at 4.01 ppm (J = 4 and 10 Hz), and a triplet for H_A^4 occurs at lower field (5.15 ppm, J = 10 Hz). In the case of the (1 → 4)-disaccharide (X), on the other hand, the H_A^3 signal is seen at lower field (5.23 ppm, d.d., J = 9.5 and 4 Hz), and H_A^4 (4.32 ppm, t, J = 9.5 Hz).

The ^{13}C NMR spectra of (VI)-(XI) show characteristic signals for C^6 of the rhamnose residues, three signals for the cyanoethylidene group, and signals for the anomeric C atoms. The α-configuration of the glycoside linkages follows from the values of the C_B^5 chemical shifts, which have values of 67.7 (VI), 67.6 (VII), 67.9 and 68.0 ppm (VIII) (cf. [7]). Further confirmation of the presence of a free hydroxyl group at C_A^4 in the (1 → 3)-disac-

*For Communication 2, see [1].

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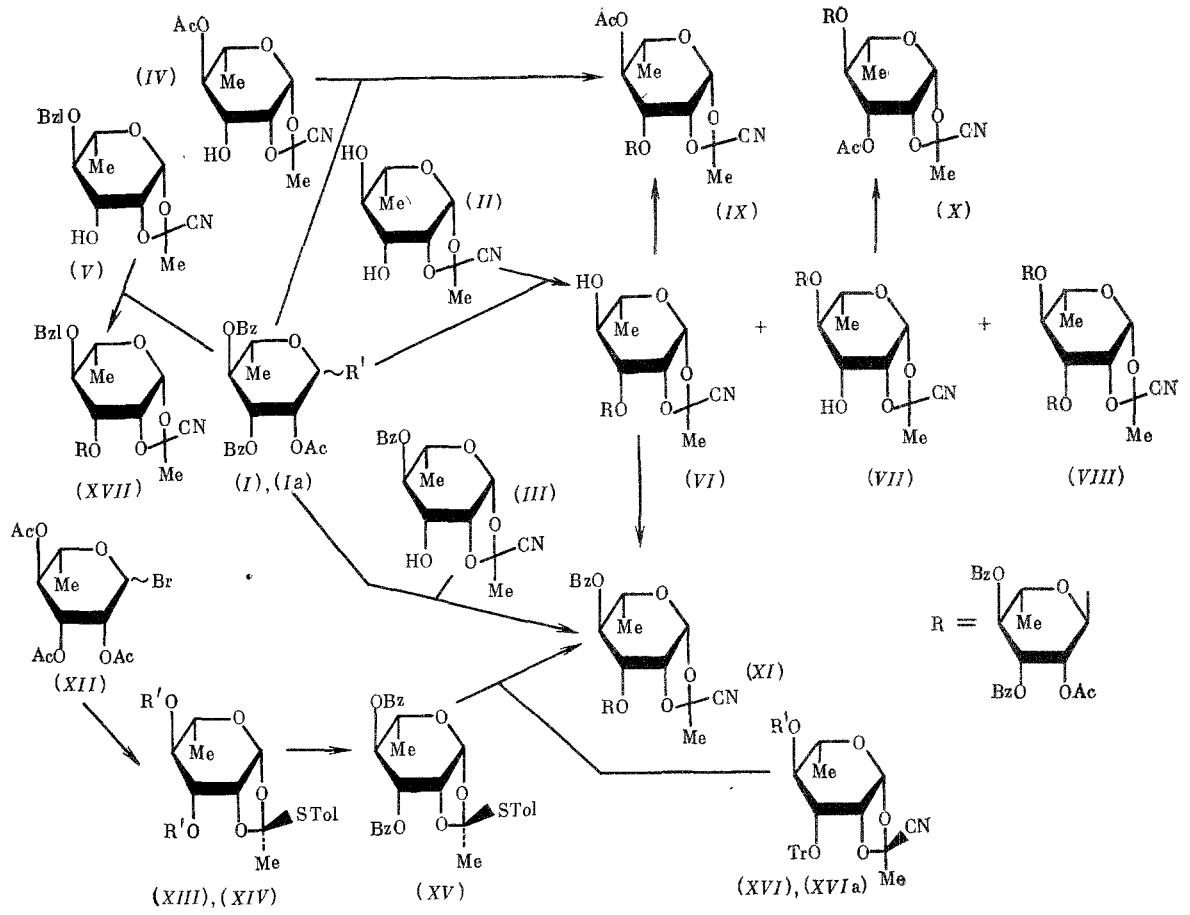
Scheme 1

R′ = Br (I);
OAc (Ia);
Ac (XIII);
H (XIV), (XVIa),
Bz (XVI).
Tol = *p*-MeC_6H_4.



charide (VI) is provided by the characteristic shift in the C_A^3 signal on acylation, i.e., when —C—C—OH → C—C—O—COR, from 81.1 in (VI) to 78.4 in (IX) or 78.3 ppm in (XI), the C_A^2 signal being unaffected. In the (1 → 4)-disaccharide (VII), which contains a hydroxyl group at C_A^3, a high-field shift in the 3 position following acetylation (the acetylation β-effect) is experienced by both "neighbors," C_A^2 and C_A^4: δ 81.2 → 78.2; 79.5 → 78.0 ppm.

The second approach to the synthesis of (XI), i.e., assembly BA, was by glycosylating the trityl ether (XVI) with the thio-orthoester (XV). This was a legitimate approach in view of the greater glycosylating activity of thio-orthoesters as compared with the corresponding CED in the glycosylation of trityl ethers in the presence of $TrClO_4$, the reaction with thio-orthoesters being virtually instantaneous [8], whereas that with the CED requires 8-16 h for completion [9]. The trityl ether (XVI) was obtained by the selective tritylation of the diol (II) as described in [3], followed by benzoylation (48% yield calculated on the diol). The thio-orthoester (XIV) was obtained by deacetylating 3,4-di-O-acetyl-1,2-O-[1-(exo-p-tolythio)ethylidene]-β-L-rhamnopyranose (XIII) [10] as described in [11], by treatment with MeONa in methanol—pyridine. The diol thio-orthoester (XIV), without further purifcation in view of its high lability [11], was benzoylated and subjected to CC to give the dibenzoate (XV) (63% yield on the diacetate (XIII)). Reaction of the thio-orthoester (XV) with the trityl ether (XVI) in the presence of a catalytic amount of $TrClO_4$ gave 37% of the disaccharide (XI), identical with the disaccharide obtained by benzoylating (VI).

The third, and most efficient approach to the synthesis of (XI) was by condensing the bromide (I) with 4-O-benzoyl-1,2-O[1-(exocyano)ethylidene]-β-L-rhamnopyranose (III), the synthesis of which has been reported [1]. Glycosylation of the alcohol (III) with 1.3 equiv. of the bromide (I) gave the crystalline disaccharide (XI), isolated directly from the reaction mixture by crystallization in 84% yield.

The aglycone component (the alcohol (III)), used in the third route to the synthesis of assembly BA, was obtained from methyl-α-L-rhamnopyranoside in seven steps [1] (as compared with four steps in the case of the diol (II)), but all seven steps take place smoothly and in high yield. CC is required only at the stage of preparation of 3-O-acetyl-4-O-benzoyl-1,2-O-(1-cyanotheylidene)-β-L-rhamnopyranose, to separate the isomers. This synthesis can

be carried out using large amounts of material with 3-4 days. The advantage conferred by the shorter synthetic route to the aglycone component (II) in the first approach to the synthesis of the BA assembly is nullified by the low yields of the required glycosylation product (VI) and the need to employ CC to isolate it from the multicomponent reaction mixture.

For purposes of comparison, we also synthesized the disaccharide (XVII), which contains a benzyl protecting group in the O^4 position of the "reducing" rhamnose residue instead of a benzoyl group, and which could serve as the starting point for further syntheses. Glycosylation of the aglycone component (V) [12] with the bromide (I) under Helferich conditions gave a 90% yield of the disaccharide (XVII), the ^{13}C NMR spectrum of which, like its analogs (VI), (IX), and (XI), contained characteristic signals confirming the structure (XVII).

EXPERIMENTAL

The methods and apparatus employed have been described previously [2].

1,2-O-[1-(exo-Cyano)ethylidene]-β-L-rhamnopyranose (II). To a solution of 2.7 g (9.03 mmoles) of 3,4-di-O-acetyl-1,2-O-[1-(exocyano)ethylidene]-β-L-rhamnopyranose (IIa) [4] in 40 ml of dry pyridine was added a solution of 0.45 ml of 1 M MeONa in 10 ml of methanol. According to TLC (alcohol–chloroform, 1:9), the reaction was complete in 5 min. The solution was neutralized with 0.6 ml of 1 M acetic acid in toluene, evaporated, co-evaporated with heptane (2 × 30 ml), and subjected to CC in the system alcohol–chloroform (up to ∿15% of alcohol), to give 1.82 g (94%) of the diol (II), mp 116-117°C (ethyl acetate–hexane), $[\alpha]_D$ −11° (C, 1.5), cf. [3].

4-O-Benzoyl-3-O-trityl-1,2-O-[1-(exocyano)ethylidene]-β-L-rhamnopyranose (XVI). The product obtained from 3.25 mmoles of (IIa) as described above (but without chromatographic purification) was dissovled in 10 ml of dichloromethane, and 0.43 ml of 2,4,6-collidine added, followed portionwise with stirring by 1.02 g (3 mmoles) of $TrClO_4$ [13]. The mxiture was stirred for 0.5 h, until the yellow color had disappeared, diluted with 50 ml of chloroform, washed with water (3 × 50 ml), dried, and the residue subjected to CC in benzene–chloroform (up to 50% chloroform) to give 0.93 g (63%) of (XVIa). The product was treated with 1.2 ml of benzoyl chloride in 10 ml of pyridine, kept for 5 days at 20°C (followed by TLC), decomposed at 0°C with 0.5 ml of water, poured into 250 ml of ice water, extracted with dichloromethane (2× 100 ml), washed with saturated $NaHCO_3$ solution, dried, evaporated, and co-evaporated with toluene. The residue was subjected to CC to give 0.87 g (48%) of (XVI) as a yellow foam, $[\alpha]_D$ +24.2° (C, 1.5). ^{13}C NMR spectrum (δ, ppm): 17.6 (C^6), 26.9 (MeCCN), 70.2, 71.6, 70.8 (C^3–C^5), 80.3 (C^2), 96.5 (C^1), 88.4 ($OCPh_3$), 101.4 (MeCCN), 116.5 (CN).

3,4-Di-O-Benzoyl-1,2-O-[1-(exo-p-tolythio)ethylidene]-β-L-rhamopyranose (XV). To a solution of 0.71 g (1.79 mmoles) of the thio-orthester (XIII) [10] in 1 ml of dry pyridine was added 1.5 ml of 0.1 M MeONa in methanol. After 5 min (the reaction was complete after this time according to TLC), 6.15 ml (53.4 mmoles) of benzoyl chloride was added at 0°C, and the mixture stirred for 2 h at 20°C. The mixture was then decomposed with 2 ml of water with cooling, poured into 200 ml of ice water, extracted with chloroform (3 × 50 ml), washed with saturated $NaHCO_3$ solution and water, dried, and evaporated. CC of the residue in the system benzene–ether gave 0.59 g (63%) of (XV). The product was crystallized by evaporating an ether–hexane solution, mp 125-127°C, $[\alpha]_D$ +159° (C, 2). PMR spectrum (δ, ppm, J, Hz): 1.30 d (3H, H^6, J = 6), 1.88 s (3H, $MeCS_{aryl}$), 2.22 s (3H, MeC_6H_4), 3.77 m (1H, H^5), 4.90 d.d. (1H, H^2), 5.45-5.67 m (3H, H^1, H^3, H^4).

3-O-(2-O-Acetyl-3,4-di-O-benzoyl-α-L-rhamnopyranosyl)-4-O-benzoyl-1,2-O[1-(exocyano) ethylidene]-β-L-rhamnopyranose (XI). a) To a solution of 0.58 g (0.95 mmole) of (VI) in 8 ml of dry pyridine was added 0.5 ml of benzoyl chloride. The mixture was kept for 72 h at 20°C (TLC), decomposed at 0°C with 0.2 ml of water, poured into 150 ml of ice water, the oil separated, dissolved in 70 ml of chloroform, the solution washed with water, saturated $NaHCO_3$, and water, dried, and evaporated. The residue was purified by CC to give 0.60 g (88.5%) of (XI), mp 197-198.5°C (methanol), $[\alpha]_D$ +102.5° (C 0.7). Found: C 63.83; H 5.21; N 1.88%. $C_{38}H_{37}NO_{13}$. Calculated: C 63.77; H 5.21; N 1.95%. ^{13}C NMR spectrum (δ, ppm): 17.5, 17.6 (C_A^6, C_B^6), 20.6 (MeCOO), 26.5 (MeCCN), 101.8 (MeCCN), 117.1 (CN), 67.8 (C_B^5), 69.3 (C_A^5), 70.2 (C_B^2, C_B^3), 71.5 (C_A^4, C_B^4), 78.3 (C_A^3), 80.3 (C_A^2), 96.9 (C_A^1, $^1J_{C,H}$ = 176 Hz, 100.3 (C_B^1, $^1J_{C,H}$ = 172.1 Hz, 169.6 (MeCO), 165.1, 165.6, 165.9 (PhCO).

b) To a solution of 0.53 g (0.94 mmoles) of (XVI) in 5 ml of dichloromethane was added 0.015 ml (0.15 mmole) of 2,4,6-collidine and 100 mg (0.3 mmole of $TrClO_4$, followed dropwise

with stirring by a solution of 0.54 g (1.04 mmoles) of the thio-orthoester (XIV) in 10 ml of dichloromethane over 20 min. The mixture was then treated with 0.5 ml of a mixture of methanol and pyridine (1:2), diluted with 20 ml of chloroform, washed with water (3 × 20 ml), evaporated, reevaporated with toluene, and the residue subjected to CC to give 250 mg (37%) of (XI), R_f 0.38 (ether–benzene, 1:4) as a foam, $[\alpha]_D$ +84.5° (C, 1.18). Its ^{13}C NMR spectrum was identical with that of the product obtained by method a) above.

c) To a suspension of the aglycone component (III) (1.72g, 5.4 mmoles) and 1.76 g (7 mmoles) of $Hg(CN)_2$ in 5 ml of acetonitrile was added with stirring a solution of the bromide (I), obtained from 7 mmoles of the acetate (Ia) as described in [2], in 10 ml of acetonitrile. The mixture was stirred for 1 h, diluted with 100 ml of chloroform, poured into 100 ml of water, the organic layer washed with 1M KBr (2 × 50 ml) and water, dried, and the residue crystallized from methanol to give 3.24 g (84%) of (XI). A further 0.35 g of (XI) was obtained from the mother liquors, total yield 93%, mp 196-197°C, $[\alpha]_D$ +105° (C, 1), the ^{13}C NMR spectrum of which was identical with that obtained above.

Glycosylation of the Diol (II). To a suspension of the crystalline diol (II) (0.88 g, 4 mmoles) and 1 g (4 mmoles) of $Hg(CN)_2$ in 3 ml of acetonitrile was added with stirring a solution of the bromide (I), obtained from 4 mmoles of the acetate (Ia), in 5 ml of acetonitrile, over 20 min, and stirring continued for 1 h at 20°C. According to TLC (ethyl acetate–benzene, 1:2), the reaction mixture contained five products, with Rf 0.66, 0.53, 0.35, 0.33, and 0.05. The mixture was treated with 0.5 ml of pyridine, diluted with 10 ml of chloroform, the solid isolated by filtration, the filtrate evaporated and the residue subjected to CC in the system alcohol–ethyl acetate–benzene (10:30:60). After the corresponding fractions had been combined, the products with R_f 0.66 and 0.53 were dissolved in chloroform, mercury salts removed by washing with 1 M KI and water, and the solution dried and evaporated to give: 1) the trisaccharide (VIII) — 3,4-di-O-(2-O-acetyl-3,4-di-O-benzoyl-α-L-rhamnopyranosyl)-1,2-O-[1-(exocyano)ethylidene]-β-L-rhamnopyranose, yield 0.17 g (4.2%), $[\alpha]_D$ +62.4° (C, 1.5), colorless foam, R_f 0.66. ^{13}C NMR spectrum (δ, ppm): 17.4, 17.6, 19.0 (C_A^6, C_B^6, C_C^6) 26.4 (MeCCN), 101.1 (MeCCN), 117.0 (CN), 20.6, 20.7 (2 MeCO), 67.9, 68.0 (C_B^5, C_C^5), 80.2, 81.1 (C_A^2, C_A^3), 97.0 (C_A^1), 99.1, 100.4 (C_B^1, C_C^1), 165.5, 165.7, 165.8 (PhCO), 169.5, 170.0 (MeCO); 2) the (1 → 4)-disaccharide (VII) — 4-O-(2-acetyl-3,4-di-O-benzoyl-α-L-rhamnopyraosyl)-1,2-O-[1-(exocyano)ethylidene]-β-L-rhamnopyranose, yield 0.49 g (20%), colorless foam $[\alpha]_D$ +14.3° (C 1.5), R_f 0.53. ^{13}C NMR spectrum (δ, ppm): 17.5, 18.4 (C_A^6, C_B^6), 20.7 (MeCOO), 26.4, 101.1, 117.0 (MeCCN), 67.6 (C_B^5), 70.2, 70.3 (×2), 71.3, 71.4 (C_A^3, C_A^5, C_B^2, C_B^3, C_B^4), 79.5 (C_A^4), 81.2 (C_A^2), 97.05 (C_A^1), 99.2 (C_B^1), 165.72, 165.78 (PhCO), 170.2 (MeCO); 3) the disaccharide (VI), contaminated with the product with R_f 0.35, yield 0.18 g; 4) the disaccharide (VI) — 3-O-(2-O-acetyl-3,4-di-O-benzoyl-α-L-rhamnopyranosyl)-1,2-O-[1-(exocyano)ethylidene]-β-L-rhamnopyranose, yield 1.02 g (41%), snow-white foam, R_f 0.33, $[\alpha]_D$ +31° (C 2.2). ^{13}C NMR spectrum (δ, ppm): 17.5, 17.7 (C_A^6, C_B^6), 20.7 (MeCO), 26.6, 101.5, 117.1 (MeCCN), 67.7 (C_B^5), 69.9, 70.3, 70.4, 71.2, 71.4 (C_A^4, C_A^5, C_B^2, C_B^3, C_B^4), 80.5 (C_A^2), 81.1 (C_A^3), 96.8 (C_A^1), 100.5 (C_B^1), 165.8 (×2) (PhCO), 170.1 (MeCO); 5) the diol (II) starting material, yield 0.26 g (30%) R_f 0.05.

When 1.5 equiv. of the bromide (I) was used in a similar experiment, the yields of products (VIII), (VII), (VI) + product with R_f 0.35 as impurity, (VI), and (II) were 10.6, 24, 13.1, 41.2, and 10.5%, respectively.

4-O-Acetyl-3-O-(2-O-acetyl-3,4-di-O-benzoly-α-L-rhamnopyranosyl)-1,2-O-[1-(exocyano) ethylidene]-β-L-rhamnopyranose (IX). a) To a suspension of 0.42 g (1.63 mmoles) of the aglycone component (IV) [1, 6] and 0.50 g (2 mmoles) of $Hg(CN)_2$ in 2 ml of acetonitrile was added a solution of the bromide (I), obtained from 2 mmoles of the acetate (Ia), in 10 ml of acetonitrile. The mixture was stirred for 2 h at 20°C, and worked up as described above for the preparation of (XI), method c). CC gave 0.92 g (86%) of the disaccharide (IX) as a colorless foam, $[\alpha]_D$ +49° (C 2.1). Found: C 60.72; H 5.36; N 2.07%. $C_{33}H_{35}NO_{13}$. Calculated: C 60.63; H 5.39; N 2.14%. PMR spectrum (δ, ppm, J, Hz): 1.25 d, 1.39 d (3H + 3H, H_A^6, H_B^6, $J_{6,5}$ = 6.5), 1.98 s (3H, MeCCN), 2.17 s (3H + 3H, 2 MeCO), 3.56 and 4.39 two d.q. (1H + 1H, H_A^5, H_B^5). 4.01 d.d. (1H, H^3), 4.65 d.d. (1H, H_A^2, $J_{2,3}$ = 4), 5.05 d (1H, H_B^1), 5.15 t (1H, H_A^4, $J_{4,5} = J_{4,3}$ = 10), 5.37 d.d. (1H, H_B^2, $J_{2,1}$ = 1.5), 5.43 d (1H, H_A^1, $J_{1,2}$ = 2), 5.60 t (1H, H_B^4, $J_{4,5}$ = 10). 5.70 d.d. (1H, H_B^3, $J_{3,4}$ = 10, $J_{3,2}$ = 3.5). ^{13}C NMR spectrum (δ, ppm): 17.4, 17.6 (CA^6, C_B^6), 20.6, 20.8 (2MeCO), 26.5, 101.8, 116.9 (MeCCN), 67.8 (C_B^5), 69.6, 70.1, 70.5, 70.8, 71.4 (C_A^4, C_A^5, C_B^2, C_B^3, C_B^4), 165.2, 165.9 (PhCO), 169.9, 170.1 (MeCO).

b) The (1 → 3)-disaccharide (VI) (100 mg) was treated with 0.5 ml of acetic anhydride in 5 ml of pyridine. After the usual workup and CC purification, there was obtained 85 mg (80%) of (IX), identical with that obtained above by method a).

3-O-Acetyl-4-O-(2-O-acetyl-3,4-di-O-benzoyl-α-L-rhamnopyranosyl)-1,2-O-[1-(exocyano) ethylidene]-β-L-rhamnopyranose (X). The (1 → 4)-disaccharide fraction with R_f 0.53 (0.8 g) was acetylated with 3 ml of acetic anhydride in 10 ml of pyridine (48 h, 20°C). TLC analysis (ethyl acetate–benzene, 1:4) showed that the greater part of the starting material with R_f 0.44 had been converted into the main product with R_f 0.67 and two minor products with R_f 0.60 and 0.44 (the product with R_f 0.44 persisted with the time of treatment with acetic in pyridine was extended). After the usual workup, CC gave the main product, diacetate (X), R_f 0.67, yield 0.72 g (85%), mp 158-159°C (ethyl acetate–ether–pentane), $[\alpha]_D$ +50° (C 1.6). Found: C 60.67; H 5.44; N 2.49%. $C_{33}H_{35}NO_{13}$. Calculated: C 60.63; H 5.39; N 2.14%. PMR spectrum (δ, ppm, J, Hz): 1.33, 1.43 two d. (3H + 3H, H_A^6, H_B^6, $J_{6,5}$ = 6), 1.90 s (3H, MeCCN), 2.15, 2.22, two s (3H + 3H, 2MeCO), 3.63 and 4.20, two m (1H + 1H, H_A^5, H_B^5), 4.32 t (1H, H_A^4, $J_{4,5}$ = 9.5), 4.70 d.d. (1H, H_A^2), 5.12 d (1H, H_B^1), 5.23 d.d. (1H, H_A^3, $J_{3,4}$ = 9.5, $J_{3,2}$ = 4), 5.38 t (1H, H_B^2, $J_{2,3} = J_{2,1}$ = 2.2), 5.45 d (1H, H_A^1, $J_{1,2}$ = 2.5), 5.55-5.65 m (2H, H_B^3, H_B^4). ^{13}C NMR spectrum (δ, ppm): 17.4, 18.5 (C_A^6, C_B^6), 20.7 (×2) (MeCO), 26.4, 101.2, 116.7,(MeCCN), 67.9 (C_B^5), 69.5, 70.4, 70.9, 71.5, 72.0 (C_A^3, C_A^5, C_B^2, C_B^3, C_B^4), 78.0, 78.2 (C_A^2, C_A^4), 97.05 (C_A^1), 99.7 (C_B^1), 165.4, 165.8 (PhCO), 169.8, 170.9 (MeCO).

3-O-(2-O-Acetyl-3,4-di-O-benzoyl-α-L-rhamnopyranosyl)4-O-benzyl-1,2-O-[1-(exocyano) ethylidene]-β-L-rhamnopyranose (XVII). To a suspension of 0.55 g (1.6 mmoles) of the aglycone component (XIV) [12] and 0.73 g (2.5 mmoles) of $Hg(CN)_2$ in 3 ml of acetonitrile was added with stirring over 20 min a solution of the bromide (I), obtained from 2.5 mmoles of the acetate (Ia), in 2 ml of acetonitrile. The mixture was then stirred for 1.5 h at 20°C, diluted with 50 ml of chloroform, washed with water, 1 M KI, and water, dried, and evaporated. CC of the residue gave 1.14 g (90.5%) of the disaccharide (XVII), mp 89-92°C (ethyl acetate–hexane), $[\alpha]_D$ +29.3° (C 1.8). Found: C 64.97; H 5.61; N 2.41%. $C_{38}H_{39}NO_{12}$. Calculated: C 65.04; H 5.60; N 1.99%. ^{13}C NMR spectrum (δ, ppm): 17.5, 17.9 (C_A^6, C_B^6), 20.7 (MeCO), 26.5, 101.4, 117.0 (MeCCN), 67.8 (C_B^5), 69.8, 70.1, 70.9, 71.2 (C_A^5, C_B^2, C_B^3, C_B^4), 76.0 ($PhCH_2$), 78.5 (C_A^3), 80.8 (C_A^2), 81.1 (C_A^4), 96.7 (C_A^1), 100.6 (C_B^1), 165.5, 165.8 (PhCO), 169.7 (CH_3CO).

CONCLUSIONS

1. O-α-L-Rhamnopyranosyl-1,2-O-cyanoethylidene-β-L-rhamnopyranoses have been synthesized by glycosylation of 1,2-O-cyanoethylidene-β-L-rhamnopyranose deriviatives.

2. The synthesis has been effected of a functionalized disaccharide for the construction of the tetrasaccharide monomer and its polycendensation in order to obtain the O-antigenic polysaccharide of the bacterium *Sh. flexneri*.

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SYNTHESIS OF THE PRINCIPAL CHAIN OF THE O-ANTIGENIC POLYSACCHARIDES OF *Shigella Flexneri*. COMMUNICATION 4.* SYNTHESIS OF 1,3-DI-O-ACETYL-4,6-DI-O-BENZOYL-2-DESOXY-2-PHTHALIMIDO-D-GLUCOPYRANOSE AND 1-O-ACETYL-2-O-(3-O-ACETYL-4,6-DI-O-BENZOYL-2-DESOXY-2-PHTHALIMIDO-β-D-GLUCOPYRANOSYL)-3,4-DI-O-BENZOYL-L-RHAMNOPYRANOSE

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We have previously described [1-3] the preparation of synthons for the rhamnose units (A, B, and C) and the BA assembly of the O-antigenic heteropolysaccharide of *Sh. flexneri*. We here describe the synthesis of derivatives of glucosamine (unit D) and glucosaminylrhamnose (assembly DC) for subsequent use in the assembly of the tetrasaccharide monomer.

The synthon for unit D, 1,3-di-O-acetyl-4,6-di-O-benzoyl-2-desoxy-2-phthalimido-D-glucopyranose (IX), was synthesized from the tetraacetate (VII). 2-Desoxy-2-(2-carboxy)-benzamido-D-glucose (XIV), the precursor of the tetraacetate (VII), was obtained as described in [4], with slight modifications, namely, in the N-acylation of glucosamine hydrochloride with one equivalent of phthalic anhydride in the presence of two equivalents of $NaHCO_3$, water was used as the solvent in place of aqueous dioxane. Also, in order to avoid decomposition of the phthalic anhydride by the second equivalent of $NaHCO_3$, the phthalic anhydride and glucosamine were added gradually, over 3-4 h. Acetylation of the crude (XIV) with acetic anhydride in pyridine gave a mixture of acetates (VII) in which the α-anomer predominated (cf. [5]). According to Lemieux et al. [6], acetylation of the triethylammonium salt of (XIV) gives mainly the β-anomer. We obtained the acetates (VII) in 53% yield from commercial glucosamine hydrochloride.

We have alreayd described [7] a convenient method for the preparation of the triol (I) directly from the bromide (VIII), obtained from the acetate (VII), by treatment with an excess of methanol, the yield of (I) following column chromatography (CC) being 56% on the starting tetraacetate (VII). A slight change in this procedure and avoiding the use of CC enabled crystalline (I) to be obtained in quantitative yield, calculated on (VII). We have previously described the synthesis of (I) by reaction of the bromide (VIII) with methanol under Helferich conditions followed by deacetylation with sodium methoxide in methanol to give a 65% yield, calculated on the bromide (VIII) [8] (Scheme 1).

Preparation of the benzylidene derivative of (I) by treatment with benzaldehyde in the presence of TsOH gives the 4,6-O-benzylidene derivative (II), which was converted into the 3-acetate (III). Treatment of (III) with aqueous CF_3COOH resulted in the smooth removal of the benzylidene protection (TLC), but during the workup, on evaporation of the solvent from the reaction mixture the benzylidene derivative was regenerated, with the result that when all the solvent had been removed the residue consisted almost entirely of the original benzylidene derivative. This difficulty was overcome by removing the benzylidene protection by treatment with methanol in nitromethane in the presence of pyridinium perchlorate, by analogy with a method which we have previously described for the detritylation and deacetonylation of sugar derivatives. In this instance, the inverse formation of the benzylidene derivative can easily be avoided by adding a few drops of pyridine before evaporation of the solvents. Following removal of the solvents, the diol (IV) was treated with benzoyl chloride in pyridine to give the 4,6-di-O-benzoyl-3-O-acetyl derivative (V). The reactions (VII) (VIII) → (I) → (II) → (III) → (IV) → (V) can be carried out without special purification at each step, the crystalline acetate (V) being thereby obtained in 83% yield on the starting tetraacetate (VII). Acetolysis of the methylglycoside (V) (1% sulfuric acid in acetic anhy-

*For Communication 3, see [1].

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