CHEMISTRY LETTERS, pp. 1183-1184, 1982. © The Chemical Society of Japan 1982

SYNTHESIS OF A TRIFURCATED TETRASACCHARIDE USING DEHYDRATIVE GLYCOSYLATION

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2,6-Di-O-(β-D-glucopyranosyl)-4-O-(α-L-rhamnopyranosyl)-D-glucopyranose was synthesized through three successive glycosylations with the benzyl-protected glycoses starting from the glycosyl acceptor, benzyl 4-O-allyl-6-O-benzoyl-3-O-benzyl-α-D-glucopyranoside.

Trifurcated structure of oligosaccharide sequences sometimes occurs in saponins[1], glycoproteins[2], and others[3] of physiological interest. However, chemical synthesis of such structures has not yet been attempted. We wish to communicate a sequential synthesis of the trifurcated tetrasaccharide, 2,6-di-O-(β-D-glucopyranosyl)-4-O-(α-L-rhamnopyranosyl)-D-glucopyranose (1), which composes Parillin[1a] and Sarsaparilloside[1b] from Radix sarsaparillae.

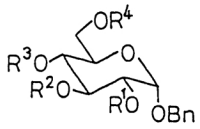
The synthesis of 1 consists of the preparation of the glycosyl acceptor 4 having two kinds of temporary protecting groups and three sets of glycosylation and deprotection. As for glycosylation, the one-stage procedure using an equimolar reagent mixture of p-nitrobenzenesulfonyl chloride, silver trifluoromethanesulfonate, and triethylamine[4] (Reagent NST) was used. It was newly found that, although the procedure favors the formation of β-glucoside, exclusive α-rhamnosylation took place in a 47% yield on the treatment of methyl 2,3,6-tri-O-benzyl-β-D-glucopyranoside[5] with 2,3,4-tri-O-benzyl-L-rhamnopyranose[6] (6, 1.3 equiv.) and Reagent NST (2.5 equiv.) in CH_2Cl_2.

Ditritylation of benzyl α-D-glucopyranoside[4b] with trityl chloride (3 equiv.) in pyridine at 70°C for 18 h selectively afforded the 2,6-ditritylate 2 (53%, mp 104-106°C, $[\alpha]_D^{20}$+48°(0.3, $CHCl_3$). After monoallylation of 2 by heating in allyl bromide containing NaH (1.5 equiv.) at 70°C and subsequent benzylation of the remaining hydroxyl group by heating in benzyl chloride containing KOH at 120°C, refluxing in $CHCl_3$-MeOH (3:2) containing trifluoroacetic acid gave benzyl 4-O-allyl-3-O-benzyl-α-D-glucopyranoside (3) (79%, mp 81-82°C, $[\alpha]_D^{20}$+131°(c 1.0, $CHCl_3$)) and the 3-O-allyl-4-O-benzyl isomer (9%, mp 94.5-95.5°C, $[\alpha]_D^{20}$+105°(c 0.3, $CHCl_3$)). The structure of 3 was confirmed by its transformation through benzylation and deallylation into benzyl 2,3,6-tri-O-benzyl-α-D-glucopyranoside, which was identified with that prepared previously[7]. Partial benzoylation of 3 with benzoyl chloride (1.0 equiv.) and pyridine at 0°C gave benzyl 4-O-allyl-6-O-benzoyl-3-O-benzyl-α-D-glucopyranoside (4) (52%, $[\alpha]_D^{20}$ +105°(c 1.0, $CHCl_3$), δ(CCl_4): 3.53(dd, $J_{1,2}$=4Hz, $J_{2,3}$=10Hz, H-2), 4.82(d, H-1)), together with the 2-O-benzoyl isomer (12%, $[\alpha]_D^{20}$+174°(c 3.1, $CHCl_3$), δ(CCl_4): 4.06(dd, $J_{2,3}$=10Hz, $J_{3,4}$=9Hz, H-3), 4.90(dd, $J_{1,2}$=4Hz, H-2), 5.12(d, H-1)).

The glucosylation of 4 (3.5 mmol) with 2,3,4,6-tetra-O-benzyl-α-D-glucopyranose (5, 1.3 equiv.) and Reagent NST (1.7 equiv.) in CH_2Cl_2 (18 ml) at 0°C overnight and subsequent chromatography on silica gel using toluene-2-butanone system as eluent gave the β(1→2)-linked disaccharide 7b (45%, $[\alpha]_D^{20}$+56°(c 5.4, $CHCl_3$), δ($CDCl_3$): 98.9 (C-1), 103.6(C-1')) and the α-anomer 7a (39%, $[\alpha]_D^{20}$+93°(c 2.3, $CHCl_3$), δ($CDCl_3$): 94.5 (C-1'), 95.2(C-1)). Debenzoylation of 7b with NaOMe in MeOH-1,4-dioxane (3:1) gave the acceptor 8 (87%, $[\alpha]_D^{20}$+67°(c 0.6, $CHCl_3$)). This was then glucosylated similarly with 5 and Reagent NST to give the branched β(1→2),β(1→6)-linked trisaccharide 9b (68%, $[\alpha]_D^{20}$+43°(c 2.6, $CHCl_3$), δ($CDCl_3$): 98.9(C-1), 103.6(C-1'→2), 104.0(C-1"→6)) and the α-anomer 9a (31%, $[\alpha]_D^{20}$+69°(c 1.7, $CHCl_3$), δ($CDCl_3$). 97.5(C-1"→6), 98.6(C-1), 103.6(C-1'-2)). Deallylation[8] of 9b furnished 10 (81%, $[\alpha]_D^{20}$+34°(c 1.1, $CHCl_3$)). The final α-rhamnosylation of 10 was achieved by the use of 6 (1.5 equiv.) and Reagent NST (3.0 equiv.) in CH_2Cl_2 afforded the totally benzylated tetrasaccharide 11 (37%, $[\alpha]_D^{20}$+19°(c 1.3, $CHCl_3$), δ($CDCl_3$): 97.9(C-1"→4), J_{CH}=167Hz), 98.8(C-1, J_{CH}=173Hz), 103.4 (C-1'→2, J_{CH}=159Hz), 104.1(C-1"'→6, J_{CH}=157Hz). The hydrogenolysis of 11 over Pd-C(10%) in moist AcOH furnished 1 (42%, mp 179-180°C, $[\alpha]_D^{20}$-16°(c 0.3, H_2O), δ(D_2O): 93.1(C-1α, J_{CH}=173Hz), 96.2(C-1β, J_{CH}=164Hz), 102.2(C-1"→4, J_{CH}=169Hz), 103.8(C-1"'→6, J_{CH}=160Hz), 105.4(C-1'→2, J_{CH}=162Hz). All the compounds synthesized gave correct analyses.

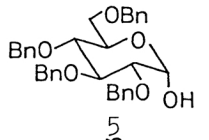
β-D-Glcp-1
↓
6
α-L-Rhap-(1→4)-D-Glcp
2
↑
β-D-Glcp-1

1

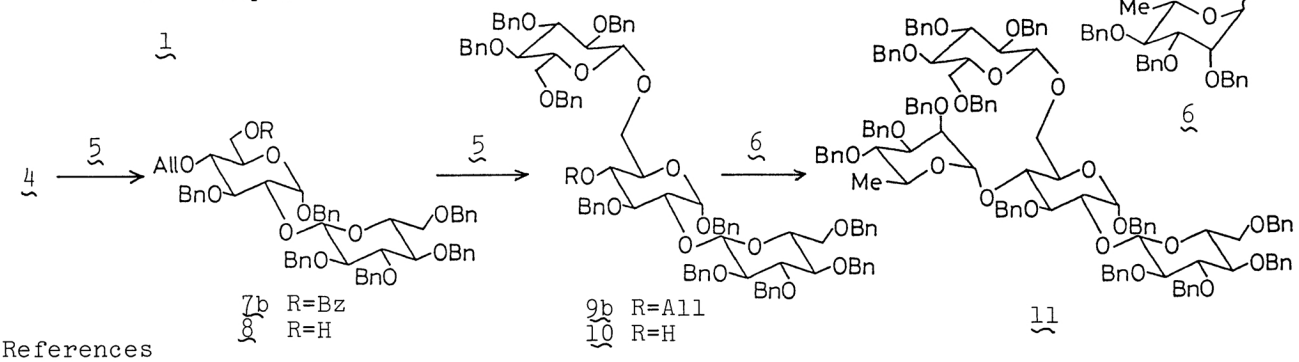


2 R^1=R^4=Tr, R^2=R^3=H
3 R^1=R^4=H, R^2=Bn, R^3=All
4 R^1=H, R^2=Bn, R^3=All, R^4=Bz

All=allyl, Bn=benzyl, Bz=benzoyl, Tr=trityl



5



7b R=Bz
8 R=H

9b R=All
10 R=H

11

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(Received May 28, 1982)