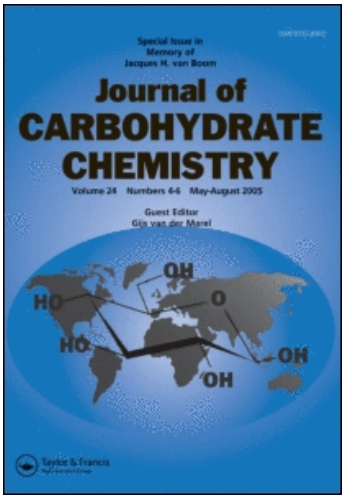

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SYNTHESIS OF SUBSTITUTED 2,6-DIOXABICYCLO [3.1.1] HEPTANES: 1,3-ANHYDRO-2,4-DI-O-BENZYL- AND 1,3-ANHYDRO-2,4-DI-O-(p-BROMOBENZYL)-β-D-RHAMNOPYRANOSE*

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ABSTRACT

The title compounds were synthesized from D-mannose in 11 steps, most of which were carried out readily in high yield. 6-Deoxygenation of methyl 2,3-O-isopropylidene-6-O-(p-tolylsulfonyl)-α-D-mannopyranoside (5) and methyl 4-O-(p-bromobenzyl)-2,3-O-isopropylidene-6-O-(p-tolylsulfonyl)-α-D-mannopyranoside (13) was carried out smoothly by direct reduction with lithium aluminum hydride in oxolane. The key intermediates for ring closure were 3-O-acetyl-2,4-di-O-benzyl- (11) and 3-O-acetyl-2,4-di-O-(p-bromobenzyl)-α-D-rhamnopyranosyl chloride (18) that were prepared by direct chlorination of the corresponding methyl rhamnopyranosides with hydrogen chloride in diethyl ether. Ring closure of the chlorides was conducted with potassium tert-butoxide in oxolane at room temperature in high yield. The 1,3-anhydro-β-D-rhamnopyranose derivatives were characterized from their ^{1}H NMR, MS, and IR spectra, and by optical rotations and elemental analyses.

INTRODUCTION

As a part of our program on the development of routes to the 2,6-dioxabicyclo[3.1.1]heptane ring system, which is found in thromoboxane A_2 (TXA_2),[1,2] one of the most active subjects in biological chemistry, we report the synthesis of 1,3-anhydro-β-D-rhamnopyranose derivatives. The synthesis of

1,3-anhydro-β-D-mannopyranose[3,4] and 1,3-anhydro-β-D-glucopyranose derivatives has been reported.[5,6] The 1,3-anhydro sugar derivatives are useful compounds for investigating the highly strained nature of the bicyclic oxetane acetal nucleus of TXA_2.

Another purpose of the present research is that the stereoregular polymerization of the title compounds can afford α-(1->3)-linked D-rhamnopyranan, a 6-deoxygenated α-(1->3)-linked D-mannopyranan. It was reported that α-(1->3)-linked L-rhamnopyranose residues appeared in several Klebsiella K and pneumococcal capsular polysaccharides.[7] It was also found that the fruit bodies of Dictyophora indusiata Fisch contain a partially acetylated linear (1->3)-α-D-mannopyranan[8] that exhibits antitumor and antiinflammatory activities. For comparison, it would be interesting to investigate the bioactivity of α-(1->3)-linked D-rhamnopyranan.

RESULTS AND DISCUSSION

Crystalline methyl 2,3-O-isopropylidene-α-D-mannopyranoside (4), obtained by a reported method,[4] was tosylated selectively at C-6 at 0 °C to afford methyl 2,3-O-isopropylidene-6-O-(p-tolylsulfonyl)-α-D-mannopyranoside (5). Treatment of 5 with lithium aluminum hydride in oxolane afforded the deoxygenated product, methyl 2,3-O-isopropylidene-α-D-rhamnopyranoside (6), which was subjected to benzylation or p-bromobenzylation. It was found that some overreduced by-products, such as methyl 2,4-di-O-benzyl-3-O-isopropyl- and methyl 3,4-di-O-benzyl-2-O-isopropyl-α-D-rhamnopyranoside formed. To improve the reaction, an alternative method was investigated for the preparation of methyl 4-O-(p-bromobenzyl)-2,3-O-isopropylidene-α-D-rhamnopyranoside (14). Thus compound 5 was p-bromobenzylated and the product reduced. The improved method afforded a higher yield and avoided any side reaction. Methyl 4-O-benzyl-α-D-rhamnopyranopyranoside (8) and methyl 4-O-(p-bromobenzyl)-α-D-rhamnopyranoside (15), obtained after mild hydrolysis of compounds 7 and 14, were etherified selectively to give methyl 2,4-di-O- benzyl- (9) and methyl 2,4-di-O-(p-bromobenzyl)-α-

D-rhamnopyranoside (16) under phase transfer conditions.[9] The excess of benzyl or p-bromobenzyl bromide in the benzylation or p- bromobenzylation was removed by steam distillation. It was necessary to neutralize hydrogen bromide formed during the distillation by adding sodium bicarbonate. Otherwise, the OMe group at C-1 in the products 7, 9, 13, and 16 would be removed. Before compounds 9 and 16 were converted into the corresponding rhamnopyranosyl chlorides with anhydrous hydrogen chloride in diethyl ether, the 3-hydroxy group had to first be protected as its acetate to avoid disaccharide formation at a later stage. Thus compounds 9 and 16 were acetylated and the products, methyl 3-O-acetyl-2,4-di-O-benzyl- (10) and methyl 3-O-acetyl-2,4-di-O-(p-bromobenzyl)-α-D-rhamnopyranoside (17), were converted into the corresponding 3-O-acetyl-2,4-di-O-benzyl- (11) and 3-O-acetyl-2,4-di-O-(p-bromobenzyl)-α-D-rhamnopyranosyl chloride (18) directly under similar conditions for the conversion of methyl 3-O-acetyl-2,4,6-tri-O-benzyl-α-D-mannopyranoside into 3-O-acetyl-2,4,6-tri-O-benzyl-α-D-mannopyranosyl chloride.[4] However, since the C-1-OMe linkage in rhamnopyranoside derivatives was more sensitive to acid than the corresponding mannopyranoside derivatives, diethyl ether, a Lewis base, was employed as the solvent instead of a 1:1 mixture of dichloromethane and acetic acid. Diethyl ether was not an affective solvent for conversion of the mannopyranoside into the corresponding mannopyranosyl chlorides.[14] Compounds 11 and 18 were found to be moisture sensitive and decomposed during monitoring the reaction by silica gel TLC. However, their formation could be monitored by analytical liquid chromatography after hydrogen chloride removal. The rhamnopyranosyl chlorides 11 and 18 were the key intermediates for the synthesis of the title compounds by a ring closure reaction. It is expected that the transition state leading to the formation of 1,3-anhydro-2,4-di-O-benzyl- (12) and 1,3-anhydro-2,4-di-O-(p-bromobenzyl-β-D-rhamnopyranose (19) from the chlorides 11 and 18 would require a $^{O}S_{2}$ conformation that is not stereochemically hindered and the ring closure should go smoothly. Our observation was consistent with that expectation. The ring closure reaction of 11 and 18 was carried out with tert-

butoxide in oxolane at room temperature readily in good yield. Compared with the corresponding 1,3-anhydromannopyranose derivative analogues, compounds 12 and 19 were more acid labile. They could not be detected by silica gel TLC and could not be purified by silica gel analytical LC since they decomposed completely on the TLC plate or mostly decomposed on the analytical LC column. Therefore, a basic column packed with Lichrosorb-NH_2 was used for the purification of 1,3-anhydrorhamnopyranose derivatives and no decomposition was observed during the purification. Pure compounds 12 and 19 were stable at -20 °C for weeks.

1,3-Anhydro-2,4-di-O-benzyl-β-D-rhamnopyranose (12) was identified from its IR, MS, and ^{1}H NMR spectra, and elemental analysis. The IR spectrum showed a strong absorption for the ether linkage and no C=C absorption band. The MS spectrum showed a parent peak of moderate intensity at 326, consistent with a molecular formula of $C_{20}H_{22}O_4$. The ^{1}H NMR spectrum of 12 had similar features to the spectrum of the mannopyranose derivative analogue except for H-6. H-1 appeared as a downfield doublet caused by long range coupling between H-1 and H-3, and H-4 as an upfield quartet by coupling between H-3 and H-4, and between H-4 and H-5. Thus the 1,3-anhydrorhamnopyranose derivatives should have a similar conformation to the corresponding 1,3-anhydromannopyranose analogues.[13] Namely, the parent rhamnopyranose ring adopts a boat $B_{2,5}$ conformation and the newly formed dioxane ring a chair $^4C_1$ conformation.

EXPERIMENTAL

General Methods. All new compounds were characterized by elemental analyses, optical rotations and ^{1}H NMR spectra. Melting points were determined in capillary tubes with a "Meltemp" apparatus and a 76 mm immersion thermometer. Optical rotations ($[\alpha]_D^{16}$) were determined in a jacketed 1 dm cell with a Perkin-Elmer Model 241 MC polarimeter. Infrared spectra were recorded with a Perkin-Elmer 125 spectrometer. Proton magnetic resonance spectra (^{1}H NMR) were recorded with a Varian XL-200 spectrometer, with chloroform-d as the solvent and tetramethylsilane (Me_4Si) as the internal

standard; chemical shifts are given in ppm. Mass spectra were obtained with a JMS-D 3005 mass spectrometer, using a direct-insertion technique to introduce the samples.

The progress of all reactions was monitored by thin layer chromatography (TLC) using one of the following solvent systems: A, pure ethyl acetate; B, ethyl acetate-petroleum ether, 1:1; C, 1:2, D, 1:3; E, 1:4. Analytical LC was carried out by use of a pump, stainless steel column packed with silica gel (10x150 mm) or Lichrosorb-NH_2 (4.6x250 mm), a differential refractometer, and ethyl acetate-petroleum ether (bp 60-90 ^{o}C) as the eluant at a flow rate of 1 to 4 mL/min. Column chromatography was conducted with silica gel (100-200 mesh) packed columns (16x240, 18x300 and 35x400 mm).

Methyl 2,3-O-isopropylidene-6-O-(p-tolylsulfonyl)-α-D-mannopyranoside (5). Methyl 2,3-O-isopropylidene-α-D-mannopyranoside (4, 24 g, 0.1 mol) was dissolved in anhydrous pyridine (150 mL) in an ice bath and a solution of p-toluenesulfonyl chloride (22 g, 0.12 mol) in pyridine (100 mL) was added dropwise within 2 h with vigorous stirring. Then the reaction was carried out at room temperature for 24 h and water (10 mL) was added to stop the reaction. The solvent was removed under reduced pressure, the residue was redissolved in dichloromethane (50 mL) and the solution was washed with hydrochloric acid (5%), and saturated bicarbonate, then dried, and concentrated. Chromatography (solvent D) yielded syrup 5 (35 g, 90.2%): $[\alpha]_D^{16}$ +33.8^{o} (c 2.4, $CHCl_3$): ^{1}H NMR δ 1.28, 1.43 (2s, 6H, CMe_2), 2.37 (s, 3H, CH_3Ph), 3.27 (s, 3H, OCH_3), 3.50 (s, 2H, H-6), 3.60-4.32 (m, 4H, H-2,3,4 and 5), 4.75 (s, 1H, H-1), 7.17-7.77 ppm (m, 4H, aromatic H).

Anal. Calcd for $C_{17}H_{24}O_8S$: C, 52.6; H, 6.18. Found: C, 52.4; H, 6.22.

Methyl 4-O-benzyl-2,3-O-isopropylidene-α-D-rhamnopyranoside (7). Compound 5 (8.55 g, 0.022 mol) was dissolved in anhydrous oxolane (20 mL) and the solution was added dropwise to a suspension of lithium aluminum hydride (1.6 g, 0.042 mol) in oxolane (160 mL). The mixture was boiled under reflux with vigorous agitation and the reaction monitored by TLC (solvent C) until all of the starting material was

consumed. The precipitate was removed by filtration and the filtrate was evaporated. The residue was extracted with dichloromethane (5x20 mL), and the organic solution washed with hydrochloric acid (5%), saturated bicarbonate, then dried and concentrated. The syrup thus obtained was dissolved in anhydrous oxolane (50 mL) and the solution was added dropwise to a mixture of oxolane (150 mL), benzyl bromide (3.54 mL, 0.04 mol), and sodium hydride (0.54 g, 0.023 mol) with vigorous agitation. The reaction was carried out under reflux for 6 h. TLC (solvent B) indicated the reaction to be complete. The precipitate was removed by filtration and the filtrate was subjected to a steam distillation at pH 8 to 10 to remove excess benzyl bromide. The residue was partitioned between water and dichloromethane, and the organic layer was dried and concentrated. Crude product 7 (4.5 g, 66.0% for two steps) was obtained as a syrup which was subjected hydrolyzed directly. Chromatography yielded pure compound 7: $[\alpha]_D^{16}$ +71.1° (c 1.5, $CHCl_3$); lit.[10] $[\alpha]_D^{25}$ +62.6° (c 3.8, acetone).

Methyl 4-O-benzyl-α-D-rhamnopyranoside (8). Crude compound 7 (4.5 g, 0.015 mol) was treated with aqueous acetic acid (35 mL, 70%) under reflux for 1 h and TLC (solvent A) indicated the reaction to be complete. The solution was concentrated to a syrup which was then extracted with dichloromethane (3x20 mL). The organic phase was washed with saturated sodium bicarbonate, then dried and concentrated to give a white solid which was purified by crystallization from ethyl acetate-petroleum ether to yield 8 (3.4 g, 87.5%): mp 105 °C; $[\alpha]_D^{16}$ +66.3° (c 5.3, $CHCl_3$); lit.[11] mp 107-109 °C; $[\alpha]_D^{25}$ +72° (c 4, $CHCl_3$).

Methyl 2,4-di-O-benzyl-α-D-rhamnopyranoside (9). To the mixture of compound 8 (500 mg, 1.7 mmol), tetrabutylammonium bromide (161 mg, 0.5 mmol), benzyl bromide (342 mg, 2 mmol) and chloroform (20 mL) was added aqueous sodium hydroxide (10%, 2 mL). The reaction was carried out under vigorous agitation at room temperature and monitored by TLC (solvent D). Upon completion (24 h), the solution was subjected to steam distillation at pH 8 to 10 to remove excess benzyl bromide and then extracted with dichloromethane (4x5 mL) repeatedly. The organic layers were combined, washed with

water (2x15 mL), then dried and concentrated. The residue was purified by column chromatography (solvent D) to give syrup 9 (530 mg, 79.6%): $[\alpha]_D^{16}$ +14.8° (c 1.9, $CHCl_3$). lit.[9] $[\alpha]_D^{25}$ -15.0° (c 1.0, $CHCl_3$) for the L-enantiomer). The ^1H NMR spectrum of compound 9 was consistent with the reported values for the L-enantiomer.[12]

Methyl 3-O-acetyl-2,4-di-O-benzyl-α-D-rhamnopyranoside (10). Compound 9 (530 mg, 1.48 mmol) was treated with acetic anhydride (3 mL) and anhydrous pyridine (6 mL) by a standard method. The reaction was quantitative and compound 10 was obtained as syrup: $[\alpha]_D^{16}$ -2.5° (c, 2.1, $CHCl_3$); ^1H NMR δ 1.36 (d, 3H, $J_{5,6}$ = 6.0 Hz, H-6), 1.98 (s, 3H, CH_3CO), 3.38 (s, 3H, OCH_3), 3.58-3.90 (m, 3H, H-2,4,5), 4.43-4.78 (m, 5H, H-1 and $2CH_2Ph$), 5.18 (m, 1H, $J_{3,4}$ = 9.0 Hz, $J_{2,3}$ = 3.2 Hz, H-3), 7.20-7.50 ppm (m, 10H, aromatic H).

3-O-Acetyl-2,4-di-O-benzyl-α-D-rhamnopyranosyl chloride (11). A solution of compound 10 (200 mg, 0.5 mmol) in dried diethyl ether (10 mL) was saturated with hydrogen chloride gas at 0 °C under a nitrogen atmosphere. After chlorination for 3 h at room temperature, the solvent was stripped off. The residue was redissolvled in dichloromethane (1 mL), and then the solvent evaporated again. This process was repeated 6 to 8 times to decrease hydrogen chloride in the product to a minimum amount. The residue was redissolved in solvent E (2x2 mL) and insoluble material was removed by filtration. The filtrate was concentrated and purified by analytical LC (solvent E) to yield syrup 11 (162 mg, 80%); $[\alpha]_D^{16}$ +51.5° (c 4.2, $CHCl_3$); ^1H NMR δ 1.31 (d, 3H, $J_{5,6}$ = 6.4 Hz, H-6), 1.95 (s, 3H, CH_3CO), 3.70 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 9.8 Hz, H-4), 4.10 (m, 2H, H-2,5), 4.55-4.80 (m, 4H, $2CH_2Ph$), 5.40 (dd, 1H, $J_{3,4}$ = 9.6 Hz, $J_{2,3}$ = 3.2 Hz, H-3), 5.95 (d, 1H, $J_{1,2}$ = 1.6 Hz, H-1), 7.29-7.66 ppm (m, 10H, aromatic H).

Anal. Calcd for $C_{22}H_{25}ClO_5$: C, 65.26; H, 6.22. Found: C, 65.15; H, 6.17.

1,3-Anhydro-2,4-di-O-benzyl-β-D-rhamnopyranose (12). Compound 11 (160 mg, 0.395 mmol) was dissolved in anhydrous oxolane (10 mL) and potassium tert-butoxide (150 mg, 1.3 mmol) was added under vigorous agitation. The reaction was carried out for 1.5 h at room temperature and the solvent was

stripped off. The residue was extracted with solvent E (3x2 mL) and the organic phase was concentrated and purified by analytical LC (Lichrosorb-NH_2) to give syrupy 12 (107 mg, 82.9%): $[\alpha]_D^{16}$ +64.3° (c 0.7, $CHCl_3$); ^1H NMR: δ. 1.38 (d, 3H, $J_{5,6}$ = 5.6 Hz, H-6), 3.80 (dd, 1H, $J_{4,5}$ = 6.8 Hz, $J_{3,4}$ = 3.2 Hz, H-4), 4.15 (m, 1H, H-5), 4.44-4.65 (m, 6H, $2CH_2Ph$ and H-2,3), 5.32 (d, 1H, $J_{1,3}$ = 4.8 Hz, H-1), 7.29-7.60 ppm (m, 10H, aromatic H); IR 1080 and 1100 cm^{-1} (C-O); MS m/z 326 M^+.

Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.62; H, 6.76

Methyl 2,3-O-isopropylidene-4-O-(p-bromobenzyl)-α-D-rhamnopyranoside (14). To a mixture of sodium hydride (300 mg, 12.5 mmol), p-bromobenzyl bromide (1.3 g, 5.2 mmol) in anhydrous oxolane (8 mL) was added dropwise a solution of compound 5 (1.3 g, 3.3 mmol) in oxolane (5 mL). The mixture was boiled under reflux with vigorous agitation. After 8 h, it was shown by TLC (solvent D) that the reaction was complete. The precipitate was removed by filtration, and the filtrate concentrated to give a syrup which was then redissolved in dichloromethane (50 mL). The organic solution was washed with hydrochloric acid (5%), and saturated bicarbonate, then dried, and concentrated to give methyl 4-O-(p-bromobenzyl)-2,3-O-isopropylidene-6-O-(p-tolylsulfonyl)-α-D-mannopyranoside (13). Compound 13 thus obtained was dissolved in dry oxolane (10 mL) and a solution of 13 was dropwise added to a suspension of lithium aluminum hydride (0.2 g, 5.3 mmol) in oxolane (20 mL). The mixture was boiled under reflux with vigorous agitation and the reaction was monitored by TLC (solvent D). Upon completion of the reaction, the precipitate was removed by filtration. The filtrate was subjected to steam distillation to remove the excess of p-bromobenzyl bromide at pH 8 to 10. The residue was partitioned between water and dichloromethane (5x10 mL). The organic layers were combined, dried and then concentrated. The white solid prepared above was purified by crystallization from diethyl ether-petroleum ether to yield 14 (1.1 g, 84.6%): mp 79-80 °C; $[\alpha]_D^{16}$ +45.1° (c 3.4, $CHCl_3$); ^1H NMR δ 1.25 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6), 1.33, 1.47 (2s, 6H, CMe_2), 3.20 (m, 1H, H-4), 3.32 (s, 3H, OCH_3), 3.50-4.27

(m, 3H, H-2,3,5), 4.56-4.80 (m,3H, CH_2Ph and H-1), 7.06-7.60 ppm (m, 8H, aromatic H).

Anal. Calcd for $C_{17}H_{23}BrO_5$: C, 52.73; H, 5.99. Found: C, 52.71; H, 5.94.

Methyl 4-O-(p-bromobenzyl)-α-D-rhamnopyranoside (15). To compound 14 (600 mg, 1.55 mmol) was added a 7:3 mixture (3 mL) of acetic acid and water. The hydrolysis procedure was the same as that used for the conversion of 7 into 8. Acetic acid and water were removed by evaporation under reduced pressure and the crude product thus obtained was purified by crystallization from ethyl acetate-petroleum ether to yield 15 (500 mg, 92.9%): $[\alpha]_D^{16}$ +52.2° (c 2.3, $CHCl_3$); mp 120-121 °C; ^1H NMR δ 1.30 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6), 2.35 (s, 2H, 2OH), 3.28 (m, 1H, H-4), 3.33 (s, 3H, OCH_3), 3.56-3.90 (m, 3H, H-2,3,5), 4.62-4.72 (m, 3H, CH_2Ph and H-1), 7.06-7.60 ppm (m, 8H, aromatic H).

Anal. Calcd for $C_{14}H_{19}BrO_5$: C, 48.43; H, 5.51. Found: C, 47.87; H, 5.36.

Methyl 2,4-di-O-(p-bromobenzyl)-α-D-rhamnopyranoside (16). To a solution of compound 15 (800 mg, 2.3 mmol), tetrabutylammonium bromide (161 mg, 0.5 mmol) and p-bromobenzyl bromide (820 mg, 3.3 mmol) in chloroform (20 mL) was added aqueous sodium hydroxide (2 mL, 5%), and the mixture was stirred for a day at room temperature. The reaction was processed and the product was purified in the same manner as used for the conversion of 8 into 9. Compound 16 was obtained as a syrup (950 mg, 74.1%): $[\alpha]_D^{16}$ +4.81° (c 5.0, $CHCl_3$); ^1H NMR δ 1.26 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6), 2.15 (s, 1H, OH), 3.26 (s, 3H, OCH_3), 3.60-4.55 (m, 9H, $2CH_2Ph$ and H-1,2,3,4,5), 7.06-7.60 ppm (m, 8H, aromatic H).

Anal. Calcd for $C_{21}H_{24}Br_2O_5$: C, 48.86; H, 4.69. Found: C, 48.70; H, 4.70.

Methyl 3-O-acetyl-2,4-di-O-(p-bromobenzyl)-α-D-rhamnopyranoside (17). Compound 16 (800 mg, 1.55 mmol) was treated with acetic anhydride (3 mL) and anhydrous pyridine (6 mL) to give compound 17 (syrup) quantitatively by the same procedure as used in the conversion of 9 into 10: $[\alpha]_D^{16}$ -12.04° (c 16.5, $CHCl_3$); ^1H NMR δ 1.28 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6), 1.97 (s, 3H, CH_3CO), 3.26 (s, 3H, OCH_3), 3.70-4.00 (m, 3H,

H-2,4,5), 4.56 (m, 5H, $2CH_2Ph$ and H-1), 5.20 (m, 1H, H-3), 7.06-7.60 ppm (m, 8H, aromatic H).

Anal. Calcd for $C_{23}H_{26}Br_2O_6$: C, 49.48; H, 4.70. Found: C, 49.64; H, 4.76.

3-O-Acetyl-2,4-di-O-(p-bromobenzyl)-α-D-rhamnopyranosyl chloride (18). Compound 17 (180 mg, 0.3 mmol) was converted into syrupy 18 by the same procedure as used for conversion of 10 into 11: yield (149 mg, 82.1%). $[\alpha]_D^{16}$ +25.6° (c 7.0, $CHCl_3$); ^1H NMR δ 1.38 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6), 1.98 (s, 3H, CH_3CO), 3.76-4.69 (m, 7H, $2CH_2Ph$ and H-2,4,5), 5.42 (m, 1H, $J_{3,4}$ = 9.2 Hz, $J_{2,3}$ = 3.6 Hz, H-3), 5.98 (d, 1H, $J_{1,2}$ = 2.2 Hz, H-1), 7.06-7.60 ppm (m, 8H, aromatic H).

Anal. Calcd for $C_{22}H_{23}Br_2ClO_5$: C, 46.96; H, 4.12. Found: C, 47.13; H, 4.15.

1,3-Anhydro-2,4-di-O-(p-bromobenzyl)-β-D-rhamnopyranose (19). To a solution of compound 18 (89 mg, 0.156 mmol) in oxolane (3 mL) was added potassium tert-butoxide (190 mg, 1.56 mmol) with vigorous agitation. The ring closure was carried out for 3 h at room temperature. Pure compound 19 was obtained as a syrup by the same procedure as used for the conversion of 11 into 12; yield (64.5 mg, 84.2%); $[\alpha]_D^{16}$ +36.6° (c 4.8, $CHCl_3$); ^1H NMR δ 1.38 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6), 3.75 (dd, 1H, $J_{4,5}$ = 6.8 Hz, $J_{3,4}$ = 3.0 Hz, H-4), 4.05-4.25 (m, 1H, H-5), 4.40-4.56 (m, 6H, $2CH_2Ph$ and H-2,3), 5.30 (d, 1H, $J_{1,3}$ = 4.2 Hz, H-1), 7.06-7.60 ppm (m, 8H, aromatic H); MS m/z 484 M^+.

Anal. Calcd for $C_{20}H_{20}Br_2O_4$: C, 49.61; H,4.16. Found: C, 49.52; H, 4.22.

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REFERENCES AND FOOTNOTES

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