with material prepared by a slightly different procedure (ref 2b).

Additions to 2-Methylene-1,3-cyclopentanedione (1): General Procedure. The sulfoxide (2, 1 mmol) was suspended in chloroform (10 mL). Pyridine (1 mL) was added, and the mixture was stirred at room temperature until all solids were dissolved (3 min). The alkene (1.2 mmol) was added to this bright yellow solution, and stirring was continued for the required time interval (see Table I). The chloroform and most of the pyridine was removed in vacuo. The residue was partitioned between CH_2Cl_2 (20 mL) and 5% H_2SO_4, and the organic phase was dried over $MgSO_4$. After concentration, the crude product was purified as noted below.

2-(5-Methoxy-3-oxo-4-pentenyl)-1,3-cyclopentanedione (5) was crystallized from ethyl acetate (73% yield): mp >230 °C dec, IR (KBr) ν 3400–2600, 1647, 1615, 1580, 1373 cm^{-1}; ^1H NMR ($CDCl_3$, pyr-d_5) δ 7.64 (1 H, d, J = 13 Hz), 5.61 (1 H, d, J = 13 Hz), 3.65 (3 H, s), 2.70 (2 H, m), 2.50 (2 H, m), 2.46 (4 H, s); ^{13}C NMR 199.8, 194.8, 162.4, 115.8, 104.6, 56.8, 38.4, 29.8, 15.2 ppm; MS, m/e 210.0880, $C_{11}H_{14}O_4$ requires 210.0892.

3-Acetoxy-2-(3-oxobutyl)cyclopent-2-en-1-one (8). The crude product from reaction of 1 with 2-[(trimethylsilyl)oxy]-propene was stirred with acetic anhydride (0.5 mL) and triethylamine (0.5 mL) for 2 h. After concentration in vacuo, the residue was taken up in dichloromethane (10 mL), washed successively with 5% H_2SO_4 (5 mL) and saturated $NaHCO_3$ (5 mL), dried over $MgSO_4$, filtered, and concentrated. The product was purified by flash chromatography (49% yield, pale yellow oil): IR (neat) ν 1770, 1706, 1662 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.77 (2 H, m), 2.6–2.1 (8 H, m), 2.30 (3 H, s), 2.10 (3 H, s); ^{13}C NMR 206.5, 204.8, 175.7, 165.9, 127.5, 39.5, 33.6, 28.7, 26.2, 20.1, 15.4 ppm; MS, m/e 210.0874, $C_{11}H_{14}O_4$ requires 210.0892.

3-Acetoxy-2-[(2-oxocyclopentyl)methyl]cyclopent-2-en-1-one (9). The crude product from 1 and 2-[(trimethylsilyl)oxy]-cyclopentene was converted to the enol acetate as for 8 and isolated by flash chromatography (pale oil, 55%): IR (neat) ν 1773, 1735, 1704, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.85 (2 H, m), 2.50 (3 H, m), 2.30 (3 H, s), 2.3–1.7 (8 H, m); ^{13}C NMR 218.9, 205.0, 176.6, 166.2, 127.2, 46.6, 37.0, 33.9, 28.9, 26.5, 20.9, 20.5, 19.9 ppm; MS, m/e 236.1057, $C_{13}H_{16}O_4$ requires 236.1048.

2-[(2-Oxocyclopentyl)methyl]-1,3-cyclopentanedione (7). The crude product from reaction of *N*-cyclopentenylmorpholine and 1 was crystallized from ethyl acetate (yield, 68%): mp 131–134 °C; IR (KBr) ν 3400–2600, 1735, 1566, 1373 cm^{-1}; ^1H NMR ($CDCl_3$, py-d_5) δ 2.50 (4 H, s), 2.7–1.5 (9 H, m); ^{13}C NMR 222.9, 207.5, 115.3, 48.2, 37.6, 30.3, 29.5, 20.6, 20.1 ppm; MS, m/e 194.0920, $C_{11}H_{14}O_3$ requires 194.0943.

2,3,4,5,6,7-Hexahydro-3,3-dimethyl-5-oxocyclopenta[*b*]-pyran-2-ol (11): white crystals from hexanes–methyl *tert*-butyl ether; yield 60%; mp 122–123 °C; IR (KBr) ν 3200, 1679, 1607 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.4 (1 H, br s), 5.1 (1 H, br s), 2.51 (4 H, s), 2.06 (2 H, s), 1.00 (6 H, s); MS, m/e 182.0953, $C_{10}H_{14}O_3$ requires 182.0943.

3,4,4a,5,6,7,8,9a-Octahydrocyclopenta[*b*]pyrano[*e*]-2*H*-pyran-6-one (15): pale oil, purified by flash chromatography (60% yield): IR (neat) ν 1696, 1630, 1147, 1080, 1026 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.43 (1 H, d, J = 2.6 Hz), 3.80 (2 H, m), 2.7–1.9 (7 H, m), 1.62 (4 H, m); ^{13}C NMR 203.7, 182.2, 112.6, 99.8, 62.0, 33.1, 30.5, 25.7, 23.6, 23.3, 21.0 ppm; MS, m/e 194.0955, $C_{11}H_{14}O_3$ requires 194.0928.

2-Ethoxy-2,3,4,5,6,7-hexahydrocyclopenta[*b*]pyran-5-one (14): viscous oil, purified by flash chromatography (70% yield): IR (neat) ν 1695, 1635, 1107, 1042 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.33 (1 H, dd, J = 3.7, 2.6 Hz), 3.91 (1 H, dq, J = 9.7, 7.1 Hz), 3.69 (1 H, dq, J = 9.7, 7.1 Hz), 2.54, (2 H, m), 2.42 (2 H, m), 2.23 (2 H, m), 1.96 (1 H, m), 1.75 (1 H, m), 1.24 (3 H, t, J = 7.1 Hz); ^{13}C NMR 203.4, 181.6, 115.0, 100.5, 64.7, 32.9, 26.1, 25.5, 14.8, 12.6 ppm; MS, m/e 182.0952, $C_{10}H_{14}O_3$ requires 182.0943.

4a-Ethoxy-2,3,6,7,8,9,9a,10-octahydro-1*H*,4a*H*-cyclopenta[*b*]cyclopenta[5,6]pyrano[3,2-*e*]pyran-1,8-dione (18): isolated by flash chromatography; white solid (71%); mp 156–157 °C; IR (KBr) ν 1706, 1647 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.01 (2 H, q, J = 7 Hz), 2.7–1.9 (13 H, m), 1.24 (3 H, t, J = 7 Hz); ^{13}C NMR 202.9, 179.1, 115.8, 115.0, 58.8, 33.5, 30.5, 25.5, 20.3, 15.0 ppm; MS, m/e 290.1138, $C_{16}H_{18}O_5$ requires 290.1154.

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Synthesis of Oligosaccharides Corresponding to the Common Polysaccharide Antigen of Group B Streptococci†,[1]

Vince Pozsgay* and Harold J. Jennings*

Division of Biological Sciences, National Research Council of Canada, Ottawa, Ontario, Canada K1A 0R6

Received January 28, 1988

To facilitate mapping of the immunodominant region of the common polysaccharide antigen of group B streptococci, tetrasaccharide 1-*O*-{2-*O*-[2-*O*-(α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl]-α-L-rhamnopyranosyl}-D-glucitol (**2**) was synthesized in a stepwise fashion, which was shown to be superior to the blockwise approach. The key glycosyl donor was methyl 2-*O*-acetyl-3,4-di-*O*-benzyl-1-thio-α-L-rhamnopyranoside (**22**), which was coupled to glycosyl acceptors via the agency of nitrosyl tetrafluoroborate. Other L-rhamnosyl donors developed were methyl 2,3,4-tri-*O*-acetyl-1-thio-α-L-rhamnopyranoside (**13**), 2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl bromide (**28**), 2-*O*-acetyl-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl bromide (**30**), and 2-*O*-benzoyl-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl bromide (**33**). Also synthesized were 1-*O*-(α-L-rhamnopyranosyl)-D-glucitol (**3**), methyl 2-*O*-(α-L-mannopyranosyl)-α-L-rhamnopyranoside (**4**), 1-*O*-[2-*O*-(α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl]-D-glucitol (**5**), and methyl 2-*O*-[2-*O*-(α-L-mannopyranosyl)-α-L-rhamnopyranosyl]-α-L-rhamnopyranoside (**6**). The effect of the anomeric sulfur atom on the ^{13}C NMR parameters is discussed.

In spite of spectacular results in the development of antibiotics and other antimicrobial agents, morbidity and mortality rates of neonatal bacterial sepsis and meningitis are significantly high.[2] Major causative organisms of these diseases are encapsulated group B streptococci, which are classified into five serotypes based on their type-specific,

† N.R.C.C. No. 29425.

(1) "Synthetic Oligosaccharides Related to Group B Streptococcal Polysaccharides. 3". Part 2: Pozsgay, V.; Jennings, H. J. *Carbohydr. Res.*, in press.

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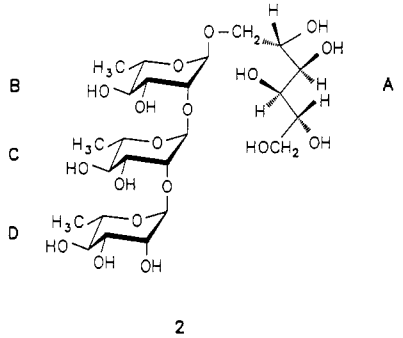
Chart I



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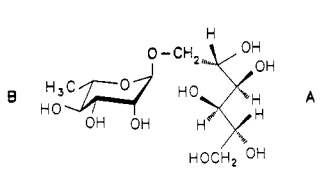

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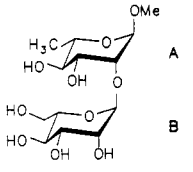

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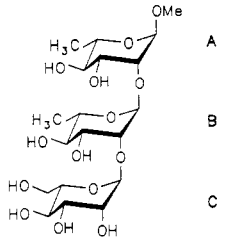

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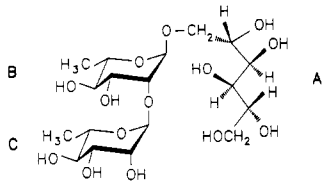

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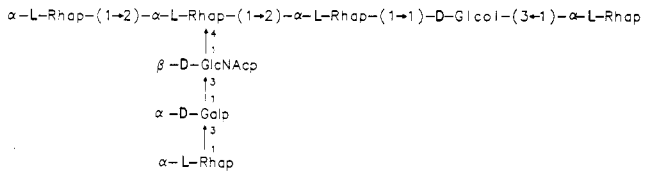
cell-surface polysaccharides.[3] On the other hand, each type is characterized by a group-specific polysaccharide antigen, common to the individual serotypes.[4] Structural studies in our laboratories have shown that the common polysaccharide antigen is highly complex in nature and is devoid of regularities characteristic of other capsular polysaccharides of this group.[5] The existence of the common polysaccharide antigen in this group is conducive to the development of a simple diagnostic procedure and also of a single, carbohydrate hapten based synthetic vaccine against all strains of group B streptococci.

Studies of the inhibition of binding of the common antigen to homologous antibodies raised in mice revealed that octasaccharide **1** isolated from the native, common poly-



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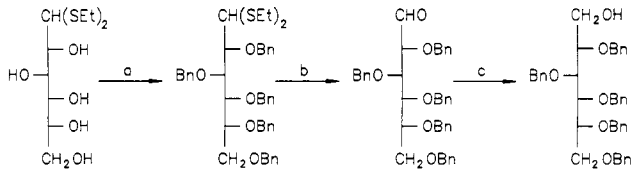
saccharide antigen represents a major, immunodominant moiety.[6] However, the precise definition of the immunodominant region of the common antigen, which is necessary for the development of a specific serodiagnostic

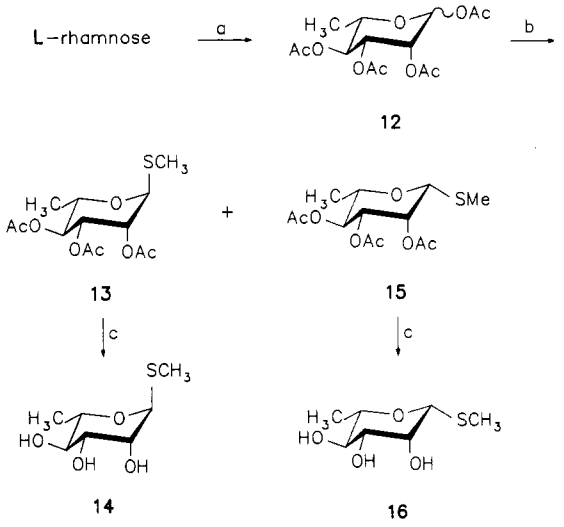
Scheme I[a]



7 8 9 10

[a] (a) $C_6H_5CH_2Br$, NaH, DMF, 4 h, 10 °C; (b) $HgCl_2$, $CdCO_3$, Me_2CO, 1 h, 25 °C; (c) $NaBH_4$, CH_3OH, 30 min, 25 °C.

Scheme II[a]



12 13 14 15 16

[a] (a) Ac_2O, C_5H_5N, 12 h, 5 °C; (b) CH_3SH, BF_3·Et_2O, CH_2Cl_2, 1 h, 0 → 15 °C; (c) $NaOCH_3$, CH_3OH, 4 h, 25 °C.

procedure, will require the acquisition of well-defined fragments of octasaccharide **1**. We have recently described[1,7] the synthesis of several fragment oligosaccharides of **1**. Herein we describe synthetic strategies for tetrasaccharide **2** and structurally related di- (**3**, **4**) and trisaccharides (**5**, **6**) (Chart I).

Results and Discussion

The overall strategy for the synthesis of **2** was based on stepwise chain elongation starting at the terminal, D-glucitol residue, thus avoiding the formation of anomeric mixtures that might be formed as a consequence of the nonparticipating[8] character of a glycosyloxy group[9] at C-2 of a glycosyl donor. Glycosyl acceptor **10** was obtained from dithioacetal **7**[10] as outlined in Scheme I.

Synthesis of the L-Rhamnosyl Donor. The α-L configuration of C-1 in unit B in **2** necessitated the use of a rhamnosyl donor having a participating group[8] at HO-2, which also had to be selectively removable after glycosidation. Stable 1,2-di-*O*-acetyl-3,4-di-*O*-benzyl-α-L-rhamnopyranose[7,11] (**11**) successfully met these requirements and was used in earlier synthetic work[7] as an efficient L-rhamnosyl donor under catalysis by trimethylsilyl trifluoromethanesulfonate (TMS-Tf). However, in this

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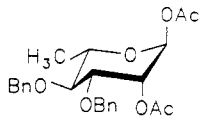
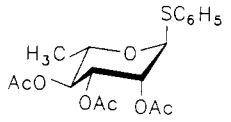


11

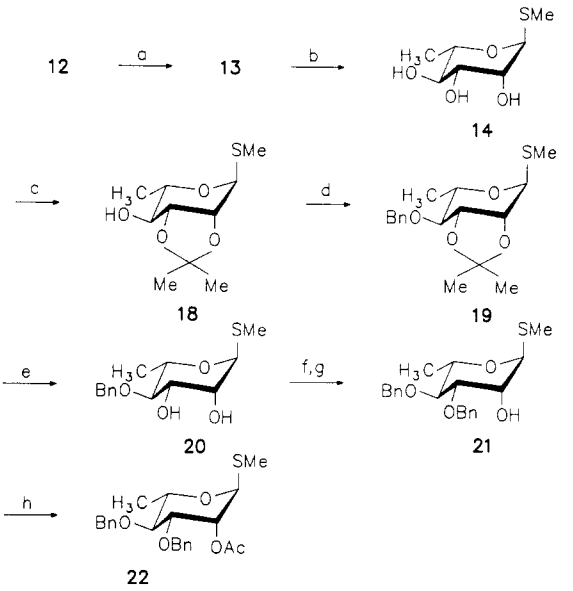
case the reaction of **10** and **11** under TMS-Tf catalysis gave a complex mixture of products, apparently because of the instability of **10** under the strongly acidic conditions of the reaction. The need for a stable rhamnosyl donor satisfying the above requirements led us to explore the potentials of thioglycoside **22**. Accordingly, L-rhamnose was converted to the known tetraacetate[12] **12**, which was treated with CH_3SH under $BF_3{\cdot}Et_2O$ catalysis in CH_2Cl_2 according to Ferrier and Furneaux[13] to give an anomeric mixture of thiorhamnosides **13** and **15** in a ratio of ca. 7:1, respectively (Scheme II). Compound **15** could be almost completely separated from **13** due to the tendency of compound **15** to crystalline, while anomer **13** obtained from the supernate did not crystallize. The anomeric configurations of compounds **13** and **15** were verified by ^{13}C NMR spectroscopy, based on the general rules[14,15] governing the stereochemical dependence of the $^1J_{C\text{-}1,H\text{-}1}$ coupling constants in hexopyranoses, which for **13** was 167 Hz, while that for **15** was 152 Hz. In the anticipation that modulation of nucleophilicity of the sulfur atom could improve the stereochemical outcome of thioglycoside formation from tetraacetate **12**, (methylthio)trimethylsilane was next selected as the donor of the methylthio group.[16] Under $BF_3{\cdot}Et_2O$ catalysis, reaction of compound **12** and $CH_3SSi(CH_3)_3$ gave thioglycoside **13** in 66% yield, while no diastereoisomer **15** could be detected in the reaction mixture.[17] The generality of this new thioglycoside synthesis is indicated by the successful conversion of peracetate **12** to phenyl thiorhamnoside **17**, using (phenylthio)trimethylsilane under $BF_3{\cdot}Et_2O$ catalysis. Thioglycoside **13** was transformed to compound **22** by analogy to the corresponding *O*-glycoside[7] (Scheme III).



17

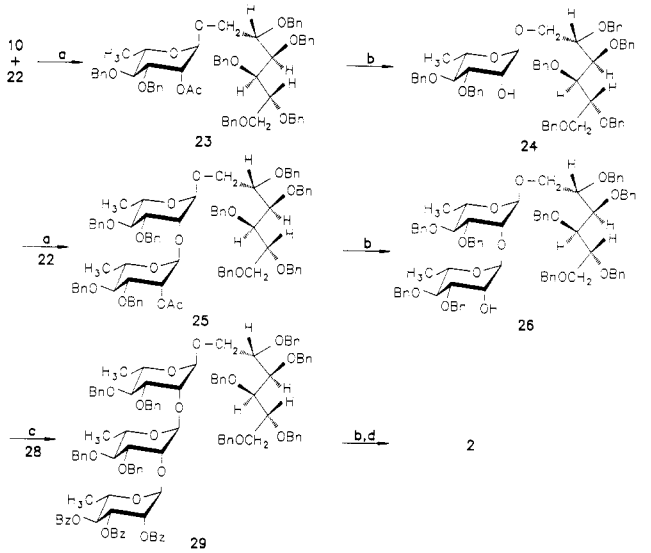
Glycosylation with Thioglycosides. Thioglycosides served as direct glycosyl donors in a number of experimental protocols, although only a few of them have proved to be practical.[18] The extreme toxicity of liquid methyl trifluoromethanesulfonate, which is the most successfully used promoter, persuaded us to develop an equally efficient but less dangerous procedure. It was thought that the thiophilicity of nitrosyl and nitronium salts[19] might make them useful reagents for thioglycoside activation. Indeed, $NOBF_4$ was found to efficiently promote disaccharide formation from thioglycosides and carbohydrate aglycons in fast, high-yielding reactions.[20] Thus, $NOBF_4$-promoted

Scheme III



[a] (a) $CH_3SSi(CH_3)_3$, $BF_3{\cdot}Et_2O$, CH_2Cl_2, 16 h, 25 °C; (b) $NaOCH_3$, CH_3OH, 4 h, 25 °C; (c) $(CH_3O)_2C(CH_3)_2$, PTS, 1 h, 25 °C; (d) $C_6H_5CH_2Br$, NaH, DMF, 2 h, 10 °C; (e) CF_3COOH, CH_3OH, 2 h, 50 °C; (f) Bu_2SnO, C_6H_6, 5 h, reflux; (g) $C_6H_5CH_2Br$, Bu_4NBr, C_6H_6, 3 h, 50 °C; (h) Ac_2O, C_5H_5N, 6 h, 25 °C.

Scheme IV[a]



[a] (a) $NOBF_4$, CH_2Cl_2, 2 h, 25 °C; (b) $NaOCH_3$, CH_3OH, 5 h, 25 °C; (c) AgOTf, $(CH_3)_2NCON(CH_3)_2$, CH_2Cl_2, 4 h, 0 → 25 °C; (d) H_2, Pd/C, EtOH, CH_3COOH, 12 h, 25 °C.

coupling of **22** with aglycon **10** in CH_2Cl_2 in the presence of 4-Å molecular sieves gave the fully protected disaccharide **23** in 68% yield (Scheme IV). The α-L configuration of the new glycoside linkage was proved by ^{13}C NMR spectroscopy ($\delta_{C\text{-}1_A}$ 99.9, $^1J_{C\text{-}1_A,H\text{-}1_A}$ = 170 Hz). Regioselective deprotection of disaccharide **23** with a catalytic amount of $NaOCH_3$ in methanol provided glycosyl acceptor **24** in 98% yield, subsequent reaction of which with donor **22** under $NOBF_4$ catalysis gave trisaccharide **25** in 62% yield. Again, the exclusive presence of α-L-interglycoside linkages in compound **25** was proven by ^{13}C NMR spectroscopy (see Experimental Section). Transesterification of **25** (Zemplén) afforded acceptor **26**. In an

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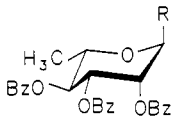
effort to avoid the frequently encountered transfer of an *O*-acetyl group from the glycosyl donor to the free hydroxyl group of the acceptor[21] under either heavy-metal[22] or Lewis-acid catalysis,[7,23] 2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl bromide[24] (**28**) was envisaged as a glycosyl donor

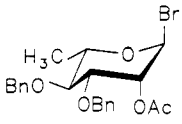


27 R=SMe
28 R=Br

for the nonreducing terminal unit in tetrasaccharide **2**. Crystalline bromide **28** was prepared from thiorhamnoside **14** by O-benzoylation (BzCl/Py) to give compound **27** followed by brominolysis, in 95% combined yield. The $^1J_{C\text{-}1,H\text{-}1}$ coupling constant in bromide **28** was 196 Hz, supporting its proposed configuration at C-1. In contrast to the highly unstable 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl bromide,[12] compound **28** showed no sign of decomposition at 20 °C for several months, thus representing another stable rhamnosyl donor, together with diacetate **11**[7] and the thiorhamnosides described herein. Coupling of bromide **28** with trisaccharide acceptor **26** (AgOTf, $(CH_3)_2NCON(CH_3)_2$) gave fully protected tetrasaccharide **29** in 66% yield.

Removal of the protecting groups from disaccharide **23**, trisaccharide **25**, and tetrasaccharide **29** using standard procedures [(i) $NaOCH_3$/MeOH; (ii) H_2–Pd/C, EtOH–AcOH] gave the free target oligosaccharides **3**, **5**, and **2**, respectively.

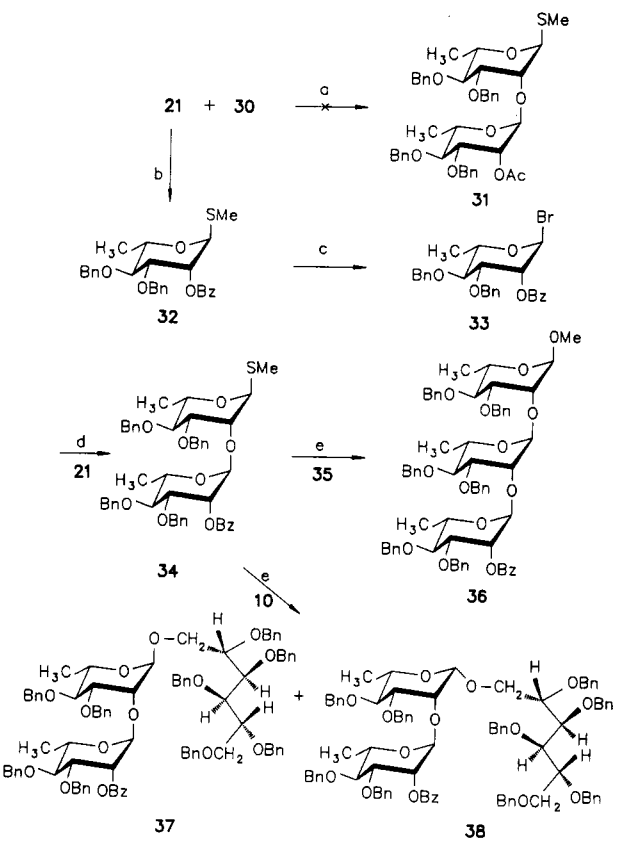
While this work was in progress, we found[20] that the $NOBF_4$-promoted reaction of methyl 4-*O*-acetyl-2,3-*O*-isopropylidene-1-thio-α-L-rhamnopyranoside with methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside gave the α-(1→4)-linked disaccharide, with no detectable amount of the β isomer. The exclusive 1,2-trans stereoselectivity was at first surprising as it was achieved without neighboring-group assistance and was thought to be governed by the anomeric effect.[8] This observation led us to hypothesize that the α-L stereochemical result of glycosylation reactions with 1-thiorhamnose-derived glycosyl donors, generated by an electrophilic activator, might not be significantly affected by the function at HO-2. A suitable candidate to test the validity of this hypothesis and its applicability to the target tetrasaccharide **2** was disaccharide **31**, in which the acetyl protecting group was required to facilitate further regioselective chain elongation (Scheme V). For the synthesis of compound **31** glycosyl bromide **30** was envisaged as the glycosyl donor. While



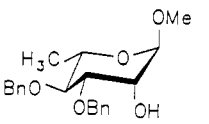
30

earlier attempts to prepare it from 1,2-di-*O*-acetyl-3,4-di-*O*-benzyl-β-L-rhamnopyranose were abortive,[25] compound **30** could be obtained simply by brominolysis of thiorhamnoside **22** in a quantitative yield. Attempted coupling of bromide **30** with thioglycoside **21** (AgOTf, $(CH_3)_2NCON(CH_3)_2$) resulted in the formation of **22**, with no practical amount of **31** being formed. To alleviate this problem, the replacement of the acetyl function by the benzoyl function was carried out.[23] Thus, compound **21** was benzoylated (BzCl/Py) to give benzoate **32** followed by brominolysis. Intermediate bromide **33** gave, in reaction with acceptor **21** (AgOTf, $(CH_3)_2NCON(CH_3)_2$) protected disaccharide **34** in 54% yield. The stereochemistry of the new glycosidic linkage was ascertained as being α-L by its $^1J_{C\text{-}1,H\text{-}1}$ coupling constant (172 Hz). Disaccharide donor **34** was then reacted with methyl 3,4-di-*O*-benzyl-α-L-rhamnopyranoside[7] (**35**) ($NOBF_4/CH_2Cl_2$) to give tri-

Scheme V[a]



[a] (a) AgOTf, $(CH_3)_2NCON(CH_3)_2$, CH_2Cl_2, 3 h, −40 → 0 °C; (b) BzCl, C_5H_5N, 2 h, 0 °C; (c) Br_2, CH_2Cl_2, 15 min, 0 °C; (d) AgOTf, $(CH_3)_2NCON(CH_3)_2$, CH_2Cl_2, 2 h, −40 → 0 °C; (e) $NOBF_4$, CH_2Cl_2, 3 h, 0 → 25 °C.

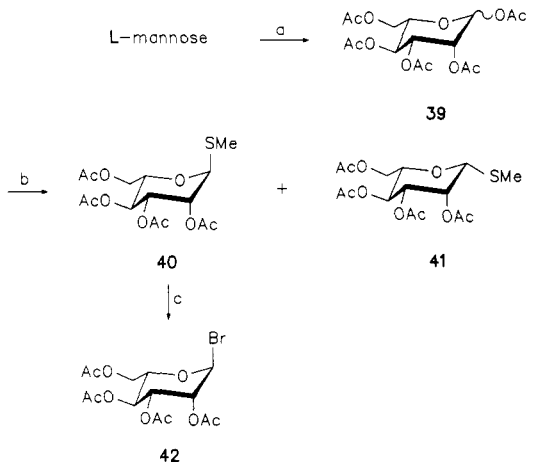


35

saccharide **36** in 36% yield. The fact that formation of β-L-linked trisaccharide was not observed in this reaction led us to use compound **34** in an alternative approach to tetrasaccharide **2**. Interestingly, reaction of thioglyoside **34** with glucitol derivative **10** ($NOBF_4/CH_2Cl_2$) gave two products in a ratio of ca. 2.5:1 in a total yield of 59%. NMR spectroscopy required the major one to be the α-L-linked product (**37**) while the minor one to be the β-L-linked product (**38**). The formation of both anomers in this reaction may be rationalized by the high reactivity, i.e., less selectivity, of the sterically unhindered primary

(21) For the mechanism of such an acetyl-group transfer Garegg and Kvarnström proposed the formation of an orthoester from glycosyl donor and acceptor followed by rearrangement (Garegg, P. J.; Kvarnström, I. *Acta Chem. Scand., Ser. B.* **1976**, *30*, 655).
(22) Kováč, P.; Glaudemans, C. P. J. *Carbohydr. Res.* **1985**, *140*, 289.
(23) Kováč, P. *Carbohydr. Res.* **1986**, *153*, 237.
(24) Ness, R. K.; Fletcher, H. G., Jr.; Hudson, C. S. *J. Am. Chem. Soc.* **1951**, *73*, 296.
(25) Josephson, S.; Bundle, D. R. *J. Chem. Soc., Perkin Trans. 1* **1980**, 297.

Scheme VI[a]

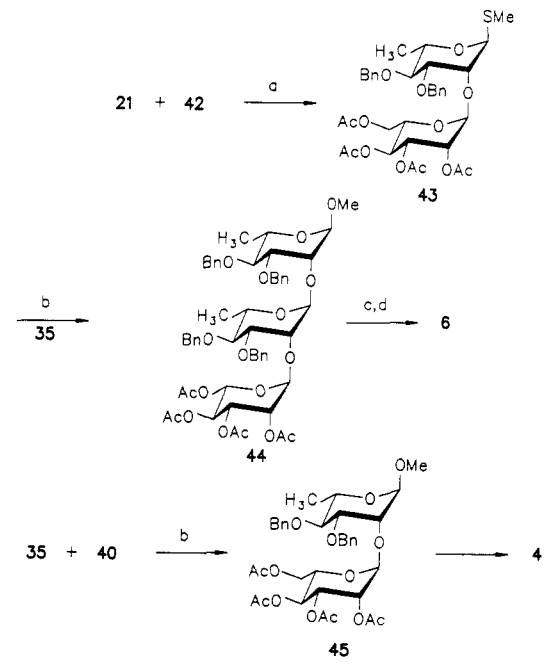


[a] (a) Ac_2O, C_5H_5N, 10 h, 5 °C; (b) $CH_3SSi(CH_3)_3$, TMS-Tf, CH_2Cl_2, 36 h, 25 °C; (c) Br_2, CH_2Cl_2, 20 min, 0 → 20 °C.

hydroxyl group in **10** vs. the much less reactive, secondary hydroxyl group in compound **35**. Although the alternative approach did provide a reasonable yield of intermediate **37** suitable for further chain elongation, the difficulty in the separation of the diastereomeric mixture **37** and **38** convincingly showed the superiority of the stepwise chain elongation strategy.

Preliminary immunochemical studies have indicated that the binding of the common polysaccharide antigen to antibodies raised against it in mice was almost equally well inhibited by tetrasaccharide **2** and the trisaccharide α-L-Rhap-(1→2)-α-L-Rhap-(1→2)-α-L-Rhap-OMe,[7] thus establishing the crucial role of the terminal, rhamnotriose sequence of the native polysaccharide in the recognition process. Further assessment of the relative importance of the individual rhamnose units and their functionalities requires the availability of structural analogues to the trirhamnoside. Next we describe the synthesis of trisaccharide **6**, which differs from the powerful trirhamnoside inhibitor only in being hydroxylated at C-6 of the nonreducing end moiety. The strategy employed followed the one used for the synthesis of compound **36**. L-Mannosyl donor **42** was obtained (Scheme VI) by brominolysis of thioglycoside **40**, which in turn was synthesized by reaction of 1,2,3,4,6-penta-*O*-acetyl-α,β-L-mannopyranose (**39**) and $CH_3SSi(CH_3)_3$ under $BF_3{\cdot}Et_2O$ catalysis. In the thioglycosylation reaction ca. 20% of 1,2-cis isomer **41** was also formed, which was at first surprising in the light of the exclusive 1,2-trans thioglycoside formation with D-glucosaminyl, D-galactosyl, and L-rhamnosyl donors.[17] The formation of the anomeric mixture of **40** and **41** can best be explained by initial formation of 1,2-trans thioglycoside **40** followed by Lewis acid catalyzed anomerization.[26,27] A test of this assumption did, indeed, reveal that $BF_3{\cdot}Et_2O$ in CH_2Cl_2 converted compound **40** into a ca. 10:1 anomeric mixture of **40** and **41**. Reaction of compound **42** with acceptor **21** (AgOTf, $(CH_3)_2NCON(CH_3)_2$) gave disaccharide **43**, having $^1J_{C\text{-}1_B,H\text{-}1_B}$ = 174 Hz. Subsequent coupling of disaccharide donor **43** with acceptor **35** ($NOBF_4/CH_2Cl_2$) gave protected trisaccharide **44**. The related disaccharide **45** was obtained by reaction of thioglycoside **40** with acceptor **35** ($NOBF_4/CH_2Cl_2$) in 52% yield. Finally, deprotection of compounds **44** and **45** as outlined above afforded hydroxylated analogues **6** and **4**

Scheme VII[a]



[a] (a) AgOTf, $(CH_3)_2NCON(CH_3)_2$, CH_2Cl_2, 4 h, −40 → 0 °C; (b) $NOBF_4$, CH_2Cl_2, 2 h, 25 °C; (c) $NaOCH_3$, CH_3OH; (d) H_2, Pd/C, CH_3COOH, EtOH, 12 h, 25 °C.

in 68% and 75% yield, respectively (Scheme VII).

NMR Spectroscopic Studies. Structures of the free di- (**3**, **4**) and trisaccharides (**5**, **6**) and that of tetrasaccharide **2** were further ascertained by complete assignment of their ^1H and ^{13}C NMR spectra (Tables I and II), using a combination of one- and two-dimensional homo- and heteronuclear correlation methods (COSY,[28] RELAY-COSY,[29] CHORTLE,[30] ^1H–^{13}C correlation spectroscopy[31]). For example, in the proton-coupled ^{13}C NMR spectrum of compound **2**, each pair of doublets centered at 101.6 and 103.0 ppm showed an additional, well-resolved splitting (Table II) characteristic[7] of the coupling across the glycosidic oxygen between the anomeric carbon atom and the proton of the "aglycon". The lines of the third doublet, centered at 99.6 ppm, exhibited no such splitting but were broadened due to coupling with two protons (H-1 and H-1′ of D-glucitol) and were assigned to C-1_B of **2**. ^{13}C–^1H correlation data required the assignment of the resonance at 4.884 ppm in the ^1H NMR spectrum to H-1_B. Sequential connectivities and heteronuclear correlation data identified all remaining resonances. An interesting feature of the ^1H–^1H COSY spectrum of compound **6** was the presence of cross peaks, due to long-range coupling, between two anomeric protons and the H-6 protons of the two rhamnose moieties, which easily identified the H-1 protons of units A and B. Further distinction between them and complete assignment were based on techniques mentioned above.

The ^{13}C NMR spectra of the thioglycosides investigated in this study exhibited 14–16 ppm upfield shifts for the anomeric carbon atom relative to their respective *O*-analogues and demonstrated that the replacement of the exocyclic O with S at C-1 have only a minimal effect on the

(26) Ogawa, T.; Matsui, M. *Carbohydr. Res.* **1977**, *54*, C17.
(27) Connolly, D. T.; Roseman, S.; Lee, Y. C. *Carbohydr. Res.* **1980**, *87*, 227.
(28) Aue, W. P.; Bartholdi, E.; Ernst, R. R. *J. Chem. Phys.* **1976**, *64*, 2229.
(29) Eich, G.; Bodenhausen, G.; Ernst, R. R. *J. Am. Chem. Soc.* **1982**, *104*, 3731.
(30) Pearson, G. A. *J. Magn. Reson.* **1985**, *64*, 487.
(31) Wilde, F. A.; Bolton, P. H. *J. Magn. Reson.* **1984**, *59*, 343.

Table I. ^{1}H NMR Data for Oligosaccharides 2–6[a]

	chemical shifts, ppm					coupling constants,[c] Hz					
H atom[b]	3	5	2	4	6	J_{H-H}	3	5	2	4	6
1A	3.626	3.631	3.629	4.892	4.775	1A–1′A	−10.8	−11.1	−10.9		
1′A	3.785	3.802	3.804			1A–2A	3.6	3.6	3.5	1.8	1.8
2A	3.967	3.963	3.966	3.958	3.908	1′A–2A	5.5	5.5	5.6		
3A	3.895	3.897	3.901	3.813	3.809	2A–3A	6.5	6.6	6.5	3.5	3.4
4A	3.627	3.622	3.619	3.461	3.460	3A–4A	2.0	2.0	2.0	9.7	9.8
5A	3.773	3.782	3.775	3.673	3.679	4A–5A	8.3	8.3	8.3	9.7	9.8
6A	3.651	3.651	3.651	1.303	1.305	5A–6A	6.2	6.2	6.1	6.3	6.3
6′A	3.828	3.838	3.829			5A–6′A	3.0	2.9	2.9		
1B	4.802	4.916	4.884	5.030	5.175	6A–6′A	−11.8	−11.8	−11.7		
2B	3.981	3.981	3.985	4.072	4.108	1B–2B	1.8	1.9	1.7	1.9	1.8
3B	3.778	3.886	3.889	3.834	3.896	2B–3B	3.5	3.4	3.4	3.4	3.4
4B	3.437	3.471	3.475	3.637	3.476	3B–4B	9.6	9.7	9.7	9.5	9.6
5B	3.700	3.770	3.709	3.69	3.762	4B–5B	9.6	9.7	9.7	9.6	9.7
6B	1.292	1.303	1.304	3.733	1.283	5B–6B	6.2	6.1	6.3	6.2	6.3
6′B				3.879		5B–6′B				1.8	
1C		4.965	5.116		5.051	6B–6′B				−12.0	
2C		4.067	4.078		4.069	1C–2C		1.9	1.7		1.9
3C		3.795	3.896		3.829	2C–3C		3.4	3.3		3.4
4C		3.447	3.478		3.657	3C–4C		9.8	9.7		9.8
5C		3.757	3.739		3.685	4C–5C		9.8	9.7		9.8
6C		1.276	1.288		3.744	5C–6C		6.3	6.3		5.4
6′C					3.858	5C–6′C					1.7
1D			4.970			6C–6′C					−12.0
2D			4.066			1D–2D			1.6		
3D			3.786			2D–3D			3.4		
4D			3.444			3D–4D			9.7		
5D			3.727			4D–5D			9.7		
6D			1.271			5D–6D			6.3		
OCH_3				3.380	3.395						

[a] In D_2O at 300 K, at 500 MHz. For other conditions, see Experimental Section. [b] For designations A–D, see Formulas 2–6. [c] First-order data.

Table II. ^{13}C NMR Data for Oligosaccharides 2–6[a]

carbon atom[b]	compound				
	3	5	2	4	6
1A	69.2	69.4	69.3	100.2 (170)	100.3 (167; 3.8)
2A	71.9	71.9	71.9	79.3	79.5
3A	70.6	70.6	70.5	70.7	70.8
4A	71.7	71.7	71.68	72.9	72.9
5A	71.7	71.8	71.72	69.3	69.4
6A	63.6	63.6	63.6	17.4	17.45
1B	100.9 (170)	99.6 (170.6)	99.6 (171.2)	103.2 (171; 4.5)	101.5 (172; 4.5)
2B	70.9	79.5	79.1	70.7	79.2
3B	71.0	70.7	70.8	71.1	70.6
4B	72.8	72.9	72.9	67.5	72.9
5B	69.6	69.9	69.8	74.1	70.0
6B	17.5	17.5	17.47[d]	61.8	17.48
1C		103.0 (170.6; 4.5)	101.6 (171.2; 4.4)		103.1 (171; 4.0)
2C		70.9	79.0		70.8
3C		70.9	70.6		71.1
4C		72.8	72.9		67.5
5C		69.8	70.0		74.1
6C		17.5	17.42[d]		61.7
1D			103.0 (171.0; 4.8)		
2D			70.8		
3D			70.8		
4D			72.8		
5D			69.9		
6D			17.42[d]		
OCH_3				55.6	55.7

[a] At 300 K, at 125 MHz for 2 and 5: at 50 MHz for 3, 4, and 6. For other conditions, see Experimental Section. [b] For designations A–D, see formulas. [c] Data in parentheses are one-bond, $^{13}C-^1H$ and three-bond, $^{13}C-O-C-^1H$ coupling constants in hertz, respectively. [d] Assignments may be interchanged.

chemical shifts of C-4 and C-6. These observations are in good agreement with those described earlier by Rao and Perlin[32] for 1-thioglucopyranosides. Extensive deshielding (7–9 ppm) of C-5 was found in 1-thio-β-L-rhamno-(**15**, **16**) and 1-thio-β-L-mannopyranosides (**41**, methyl 1-thio-β-L-mannopyranoside[33]) relative to C-5 of the corresponding α-anomers (**13**, **14**, **40**, methyl 1-thio-α-L-mannopyranoside[34]). The magnitude of the corresponding de-

(32) Rao, V. S.; Perlin, A. S. *Carbohydr. Res.* **1981**, *92*, 141.

(33) Methyl 1-thio-β-L-mannopyranoside was obtained from compound **41** by transesterification (Zemplén). ^{13}C NMR (D_2O) δ 86.7 (C-1, $J_{C-1,H-1}$ = 155 Hz), 81.1 (C-5), 74.6 (C-3), 72.7 (C-2), 67.5 (C-4), 61.9 (C-6), 14.4 (SCH_3).

shieldings in *O*-glycosides[35] is 4–5 ppm for C-5 and 2–3 ppm for C-3.[36] A comparison of the chemical shifts for C-3 and C-5 of methyl 1-thio-β-L-rhamnopyranoside (**16**) with those of 1,5-anhydro-L-rhamnitol[37] demonstrates that the β-methylthio group has only a negligible effect on the chemical shift of these carbon atoms (0.5 ppm or less), which are located γ-antiperiplanar to the heteroatom. This observation is further proof for the lack of a γ-anti effect by the bivalent sulfur atom, first demonstrated in carbocycles by Eliel et al.[38] and in 1-thioglucopyranosides by Rao and Perlin.[32] On the other hand, in methyl 1-thio-α-L-rhamnopyranoside (**14**) the methylthio group causes upfield displacements of 2.4 ppm for C-3 and 7.9 ppm for C-5 relative to 1,5-anhydro-L-rhamnitol.[37] These shifts are nearly identical with those of the methoxy group in methyl α-L-rhamnopyranoside[36] relative to 1,5-anhydro-L-rhamnitol[37] and are indicative of comparable γ-gauche effects for sulfur and oxygen. A comparison of the chemical shifts of methyl 2,3,4-tri-*O*-acetyl-1-thio-α- (**13**) and -β-L-rhamnopyranoside (**15**) with those of 2,3,4-tri-*O*-acetyl-1,5-anhydro-L-rhamnitol[39] provides a further example of the lack of any significant γ-anti effect of sulfur in carbohydrates. Recently, Szilágyi and Györgydeák[40] gave ample evidence for the similar behavior of the azido substituent at C-1 of hexopyranoses. Furthermore, it is noteworthy that the value of $^1J_{C\text{-}1,H\text{-}1}$ coupling constants in β-thioglycosides **15** and **16** is 6–8 Hz lower (152–154 Hz) than in the corresponding *O*-glycosides[36] (160 Hz), whereas this difference for the corresponding α anomers is only 1–4 Hz. Previously, the lower value of $^1J_{C\text{-}1,H\text{-}1}$ coupling constants in thioglycosides had been attributed[15] to electronegativity differences between sulfur and oxygen. This term seems to account, however, for only ca. 1–4 Hz of the difference, as manifested in the α series. In β-thioglycosides the unusually low value of the $^1J_{C\text{-}1,H\text{-}1}$ coupling constant is probably a cooperative result of the lower electronegativity of sulfur relative to oxygen and bond-angle effects, which were shown to influence the $^1J_{C,H}$ values (cf. ref 40). It is, indeed, plausible to assume that unfavorable lone-pair interactions between O-5 and the anomeric (β) sulfur atom change the orientation of H-1 relative to its position in *O*-glycosides. On the basis of the linear correlation between the magnitude of $^1J_{C,H}$ coupling constants and the distance of the proton from neighboring lone-pair electrons (cf. ref 15), the H_1–C_1–C_2 bond angle is probably smaller in 1-thio-β-hexopyranosides than in the corresponding *O*-glycosides.

Experimental Section

Melting points were taken on a Fisher-Johns apparatus and are not corrected. Optical rotations were measured with a Perkin-Elmer 243 automatic polarimeter at ambient temperatures (22–25 °C). All glycosylation reactions were carried out under nitrogen. Column chromatography was made on silica gel 60 (0.040–0.063 mm, E. Merck). Eluents of Sephadex chromatography were analyzed with a Waters R-403 differential refractometer. ^1H and ^{13}C NMR spectra were run on a Bruker AM-500 and AM-200 spectrometer at 500 and 50 MHz, respectively, at 300 K, unless stated otherwise, using standard Bruker DISNMR software. Internal references: acetone (2.225 ppm for protons or 31.07 ppm for carbons in D_2O), $CDCl_3$ (77.0 ppm for the central line of its triplet of carbons in $CDCl_3$). ^1H NMR assignments are definitive. ^{13}C NMR assignments given for **2–6**, **13–22**, **27**, **28**, **30**, **32**, **40**, **41**, methyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside,[36] methyl 2,3,4-tri-*O*-acetyl-β-L-rhamnopyranoside,[36] methyl α-L-rhamnopyranoside,[36] methyl β-L-rhamnopyranoside,[36] methyl 1-thio-α-L-mannopyranoside,[34] methyl 1-thio-β-L-mannopyranoside,[33] 1,5-anhydro-L-rhamnitol,[37] and 2,3,4-tri-*O*-acetyl-1,5-anhydro-L-rhamnitol[39] are definitive, and others are tentative. Compounds **2–6** were freeze-dried from 99.5% D_2O twice before NMR measurements in 99.95% D_2O.

2,3,4,5,6-Penta-*O*-benzyl-D-glucose Diethyl Dithioacetal (8). A stirred solution of diethyl dithioacetal **7**[10] (6 g, 21 mmol) in 100 mL of dry DMF was treated with 10 g of sodium hydride (50% dispersion in oil (208 mmol). The mixture was stirred for 1 h at 25 °C, cooled to 10 °C, and treated dropwise with 25.9 g of benzyl bromide (18 mL, 151 mmol). The reaction mixture was stirred at 10 °C for 4 h, then treated dropwise with 20 mL of MeOH, and partitioned between chloroform and water. The organic layer was dried (Na_2SO_4) and concentrated. Chromatography of the residue with 1:10 ethyl acetate–hexane as eluant gave compound **8** (14.2 g, 92%); $[\alpha]_D$ −0.7° (*c* 2.5, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 138.7, 138.6 (2×), 138.3 (2×) (aromatic quaternary carbons), 128.2–127.2 (aromatic carbons), 82.8, 80.9, 79.4, 78.9 (C-2,3,4,5), 75.2, 74.5, 73.5, 73.2, 71.9 [CH_2 (Bn)], 70.1 (C-6), 53.6 (C-1), 24.9 (2×) (CH_2CH_3), 14.3, 14.2 (2 CH_3CH_2).

2,3,4,5,6-Penta-*O*-benzyl-D-glucose (9). A solution of compound **8** (0.9 g, 1.2 mmol) in 20 mL of acetone was treated with $HgCl_2$ (2 g, 4.2 mmol) and $CdCO_3$ (3 g, 1.74 mmol), and the mixture was stirred at 25 °C for 1 h. The mixture was filtered and the filtrate was concentrated. The residue was treated with 20 mL of chloroform, the mixture was filtered, and the filtrate was extracted with 1% aqueous KI (2 × 5 mL) and water (5 mL), dried (Na_2SO_4), and concentrated to give aldehyde **9** as an oil (0.72 g, 93.5%): $[\alpha]_D$ +6.2° (*c* 1.6, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 200.6 (C-1), 138.4, 138.1, 137.9, 137.7, 137.3 (aromatic quaternary carbons), 128.3–127.5 (aromatic carbons), 80.9, 80.0, 78.2, 77.2 (C-2,3,4,5), 74.0, 73.6, 73.3, 73.0, 71.7 [CH_2 (Bn)], 68.5 (C-6).

2,3,4,5,6-Penta-*O*-benzyl-D-glucitol (10). A solution of 7.5 g (11.9 mmol) of aldehyde **9** in 300 mL of methanol was treated with 600 mg (15.8 mmol) of sodium borohydride at 25 °C for 30 min. Excess reagent was decomposed by dropwise addition of 2 mL of glacial acetic acid. The solution was concentrated, and the syrupy residue was partitioned between chloroform and water. The organic phase was dried (Na_2SO_4) and concentrated to give syrupy **10** (6.95 g, 92.4%): $[\alpha]_D$ −1.5° (*c* 0.7, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 138.6, 138.4, 138.2 (2×) (aromatic quaternary carbons), 128.4–127.4 (aromatic carbons), 79.3 (2×), 79.0, 78.6 (C-2,3,4,5), 74.6, 73.8, 73.3, 72.6, 71.9 [CH_2 (Bn)], 69.4 (C-6), 61.7 (C-1).

Methyl 2,3,4-Tri-*O*-acetyl-1-thio-α-L-rhamnopyranoside (13) and Methyl 2,3,4-Tri-*O*-acetyl-1-thio-β-L-rhamnopyranoside (15). A solution of peracetate **12**[11,12] (70 g, 211 mmol) in 400 mL of dry dichloroethane was treated with CH_3SH (ca. 12 mL) and BF_3·Et_2O (100 mL) at 0 °C. The mixture was allowed to reach 25 °C in 1 h and was then neutralized with saturated, aqueous $NaHCO_3$, washed with water, dried (Na_2SO_4), and concentrated. Spontaneous crystallization of the residual syrup was aided by addition of diethyl ether (150 mL). Filtration gave

(34) Methyl 1-thio-α-L-mannopyranoside was obtained from compound **40** by transesterification (Zemplén). ^{13}C NMR (D_2O) δ 86.6 (C-1, $J_{C\text{-}1,H\text{-}1}$ = 168 Hz), 73.7 (C-5), 72.3 (C-2), 71.9 (C-3), 67.9 (C-4), 61.7 (C-6), 13.7 (SCH_3).

(35) In *O*-glycosides, increased shielding of C-3 and C-5 in the α anomers was associated with 1,3-cis diaxial interactions: Perlin, A. S. In *MTP International Review of Science, Organic Chemistry, Series Two, Carbohydrates*; Aspinall, G. O., Ed.; Butterworths: London, Boston, 1977; Vol. 7, p 1.

(36) ^{13}C NMR data: methyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside ($CDCl_3$), δ 168.9 (2×), 168.8 (CH_3CO), 97.7 (C-1, $^1J_{C\text{-}1,H\text{-}1}$ = 171 Hz), 70.0 (C-4), 68.9 (C-3), 68.3 (C-2), 65.4 (C-5), 54.0 (OCH_3), 19.7 (3×) (CH_3CO), 16.5 (C-6); methyl 2,3,4-tri-*O*-acetyl-β-L-rhamnopyranoside ($CDCl_3$) δ 170.3, 170.0, 169.7 (CH_2CO), 99.4 (C-1, $^1J_{C\text{-}1,H\text{-}1}$ = 160 Hz), 71.0, 70.6 (C-3,4), 70.4 (C-5), 68.2 (C-2), 57.2 (OCH_3), 20.7 (2×), 20.5 (CH_3CO), 17.3 (C-6); methyl α-L-rhamnopyranoside (D_2O), δ 101.7 (C-1, $^1J_{C\text{-}1,H\text{-}1}$ = 170 Hz), 72.8 (C-4), 71.0 (C-3), 70.8 (C-2), 69.2 (C-5), 55.5 (OCH_3), 17.5 (C-6); methyl β-L-rhamnopyranoside (D_2O), δ 101.8 (C-1, $^1J_{C\text{-}1,H\text{-}1}$ = 160 Hz), 73.5 (C-3), 73.0, 72.8 (C-4,5), 71.2 (C-2), 57.6 (OCH_3), 17.5 (C-6).

(37) 1,5-Anhydro-L-rhamnitol was obtained by desulfurization (Raney nickel, EtOH, reflux) of **16**. ^{13}C NMR (D_2O) δ 77.7 (C-5), 74.0 (C-3), 73.2 (C-4), 70.5 (C-1), 69.9 (C-2), 17.9 (C-6).

(38) Eliel, E. L.; Bailey, W. F.; Kopp, L. D.; Willer, R. L.; Grant, D. M.; Bertrand, K. A.; Cristensen, D, K.; Dalling, D. K.; Duck, M. W.; Wenkert, E.; Shell, F. M.; Cochran, D. W. *J. Am. Chem. Soc.* **1975**, *97*, 322.

(39) 2,3,4-Tri-*O*-acetyl-1,5-anhydro-L-rhamnitol was obtained by acetylation (Ac_2O/Py) of 1,5-anhydro-L-rhamnitol.[37] ^{13}C NMR ($CDCl_3$) δ 170.2, 170.0, 169.7 (CH_3CO), 74.9 (C-5), 71.5 (C-3), 70.9 (C-4), 68.9 (C-2), 67.7 (C-1), 20.8, 20.5 (2×), (CH_3CO), 17.6 (C-6).

(40) Szilágyi, L.; Györgydeák, A. *Carbohydr. Res.* **1985**, *143*, 21.

thioglycoside **15** (8.9 g, 13.2%): mp 180–183 °C; $[\alpha]_D$ +56° (*c* 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 5.513 (dd, 1 H, $J_{1,2}$ = 1.1 Hz, $J_{2,3}$ = 3.5 Hz, H-1), 5.094 (t, 1 H, $J_{3,4} = J_{4,5}$ = 10.1 Hz, H-4), 5.022 (dd, 1 H, H-3), 4.667 (d, 1 H, H-1), 3.559 (dq, 1 H, H-5), 2.257 (s, 3 H, SCH_3), 2.184, 2.055, 1.979 (3 s, 3 × 3 H, 3 CH_3CO), 1.298 (d, 3 H, $J_{5,6}$ = 6.2 Hz, H-6); ^{13}C NMR ($CDCl_3$) δ 170.2, 170.1, 169.7 (3 $COCH_3$), 83.3 (C-1, $J_{C\text{-}1,H\text{-}1}$ = 152 Hz), 75.0 (C-5), 71.6 (C-3), 70.4 (2×) (C-2,4), 20.7, 20.6 (2×) (3 CH_3CO), 17.6 (C-6), 14.3 (SCH_3). Anal. Calcd for $C_{13}H_{20}O_7S$ (320.35): C, 48.74; H, 6.29; S, 10.01. Found: C, 48.91; H, 6.32; S, 9.91.

The mother liquor was left standing at 25 °C over the weekend. Thin-layer chromatography (3:2 ethyl acetate–hexane) indicated that the slightly acidified solution contained, exclusively, the faster moving compound (**13**). Concentration of the solution gave syrupy **13** (52 g, 77.0%): $[\alpha]_D$ −117° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz) δ 5.350 (dd, 1 H, $J_{1,2}$ = 1.5 Hz, $J_{2,3}$ = 3.3 Hz, H-2), 5.242 (dd, 1 H, $J_{3,4}$ = 10.0 Hz, H-3), 5.096 (t, 1 H, H-4), 5.086 (dd, 1 H, $J_{1,5}$ = 0.6 Hz, H-1), 4.200 (ddq, 1 H, $J_{4,5}$ = 9.4 Hz, H-5), 2.157 (s, 3 H, SCH_3), 2.151, 2.059, 1.986 (3 s, 3 × 3 H, 3 CH_3CO), 1.247 (d, 3 H, $J_{5,6}$ = 6.3 Hz, H-6); ^{13}C NMR ($CDCl_3$) δ 169.9 (3×) (3 $COCH_3$), 83.4 (C-1, $J_{C\text{-}1,H\text{-}1}$ = 167 Hz), 71.1 (2×) (C-2,4), 69.4 (C-3), 66.9 (C-5), 20.8, 20.7, 20.6 (3 CH_3CO), 17.4 (C-6), 13.7 (SCH_3).

Methyl 2,3,4-Tri-*O*-acetyl-1-thio-α-L-rhamnopyranoside (13). A mixture of peracetate **12** (950 mg, 2.86 mmol), $CH_3SSi(CH_3)_3$ (2.0 mL, 1.69 g, 14.1 mmol), powdered, 4-Å molecular sieves (~1 g), and dichloromethane (10 mL) was stirred for 1 h at 25 °C and was then treated with 40% $BF_3{\cdot}Et_2O$ (650 μL). The mixture was stirred for 36 h and filtered, and the filter cake was washed with dichloromethane (3 × 10 mL). The solution was extracted with aqueous, ice-cold $NaHCO_3$, dried (Na_2SO_4), and concentrated. The residue was chromatographed with 4:1 hexane–ethyl acetate as eluant to give syrupy **13** (610 mg, 66.6%), which was indistinguishable from **13** as obtained above.

Methyl 1-Thio-α-L-rhamnopyranoside (14). A solution of triacetate **13** (6.4 g) in 35 mL of anhydrous methanol was treated with a catalytic amount of sodium methoxide at 25 °C for 4 h. The solution was neutralized (Dowex 50W, H^+), filtered, and concentrated. Syrupy **14** (3.8 g, 98%) was crystallized from ethyl acetate–diethyl ether: mp 99–100 °C; $[\alpha]_D$ −185° (*c* 1.2, H_2O); ^1H NMR (D_2O) δ 5.132 (dd, 1 H, $J_{1,2}$ = 1.6 Hz, $J_{1,5}$ = 0.6 Hz, H-5), 4.056 (dd, 1 H, $J_{2,3}$ = 3.5 Hz, H-2), 4.012 (ddq, 1 H, H-5), 3.746 (dd, 1 H, $J_{3,4}$ = 9.1 Hz, H-3), 3.465 (t, 1 H, H-4), 2.151 (s, 3 H, SCH_3), 1.307 (d, 3 H, $J_{5,6}$ = 6.3 Hz, H-6); ^{13}C NMR (D_2O) δ 86.7 (C-1, $J_{C\text{-}1,H\text{-}1}$ = 169 Hz), 73.2 (C-4), 72.5 (C-2), 71.6 (C-3), 69.8 (C-5), 17.5 (C-6), 13.9 (SCH_3). Anal. Calcd for $C_7H_{14}O_4S$ (194.24): C, 43.27; H, 7.26; S, 16.50. Found: C, 43.01; H, 7.38; S, 16.29.

Methyl 1-Thio-β-L-rhamnopyranoside (16). Thioglycoside **15** was deacetylated as described for compound **13**. Removal of solvent left crystalline **16** in 96% yield: mp 152–154 °C; $[\alpha]_D$ +97° (*c* 1.3, H_2O); ^1H NMR (D_2O) δ 4.725 (d, 1 H, $J_{1,2}$ = 1.1 Hz, H-1), 4.012 (dd, 1 H, $J_{2,3}$ = 2.8 Hz, H-2), 3.579 (dd, 1 H, $J_{3,4}$ = 9.3 Hz, H-3), 3.409 (dq, H-5), 3.359 (t, 1 H, $J_{4,5}$ = 9.3 Hz, H-4), 2.203 (s, 3 H, SCH_3), 1.283 (d, 3 H, $J_{5,6}$ = 5.9 Hz, H-6); ^{13}C NMR (D_2O) δ 86.7 (C-1, $J_{C\text{-}1,H\text{-}1}$ = 154 Hz), 77.2 (C-5), 74.3 (C-3), 72.9 (C-2), 72.7 (C-4), 17.7 (C-6), 14.5 (SCH_3). Anal. Calcd for $C_7H_{14}O_4S$ (194.24): C, 43.27; H, 7.26; S, 16.50. Found: C, 43.22; H, 7.31; S, 16.40.

Phenyl 2,3,4-Tri-*O*-acetyl-1-thio-α-L-rhamnopyranoside (17). A mixture of peracetate **12** (913 mg, 2.74 mmol), $C_6H_5SSi(CH_3)_3$ (2.0 mL, 1.92 g, 10.6 mmol), 200 μL of 40% $BF_3{\cdot}Et_2O$, and 8 mL of dry dichloromethane was stirred at 25 °C for 12 h. The solution was treated with triethylamine (1 mL), diluted with dichloromethane (50 mL), and extracted with water. The organic layer was dried (Na_2SO_4) and concentrated. Chromatography of the residue with 1:2 ethyl acetate–hexane as eluant gave starting compound **12** (320 mg) and thioglycoside **17** (451 mg, 66.1%, based on recovery) as a crystalline solid: mp 116–118 °C; $[\alpha]_D$ −107° (*c* 1.8, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.49–7.45, 7.33–7.26 (m, 5 H, aromatic protons), 5.498 (dd, 1 H, $J_{1,2}$ = 1.6 Hz, $J_{2,3}$ = 3.3 Hz, H-2), 5.410 (d, 1 H, H-1), 5.289 (dd, 1 H, $J_{3,4}$ = 10.0 Hz, H-3), 5.146 (t, 1 H, $J_{4,5}$ = 9.9 Hz, H-4), 4.361 (dq, 1 H, H-5), 2.140, 2.076, 2.010 (3 s, 3 × 3 H, 3 CH_3CO), 1.246 (d, 3 H, $J_{5,6}$ = 6.3 Hz, H-6); ^{13}C NMR ($CDCl_3$) δ 169.9 (2×), 169.8 ($COCH_3$), 133.2 (aromatic quaternary carbon), 131.8, 129.1, 127.8 (aromatic carbons), 85.6 (C-1, $J_{C\text{-}1,H\text{-}1}$ = 169 (Hz), 71.2 (C-2), 71.0 (C-4), 69.3 (C-3), 67.7 (C-5), 20.8, 20.7, 20.6 (CH_3CO), 17.2 (C-6).

Methyl 2,3-*O*-Isopropylidene-1-thio-α-L-rhamnopyranoside (18). A mixture of triol **14** (25 g, 128.7 mmol), 2,2-dimethoxypropane (150 mL), and toluenesulfonic acid (250 mg) was stirred at 25 °C for 1 h, treated with triethylamine (1 mL), and concentrated. The residual syrup was partitioned between chloroform and water. The chloroform layer was dried (Na_2SO_4) and concentrated to give syrupy **18** (29 g, 96.2%), which crystallized on standing: mp 82–83 °C; $[\alpha]_D$ −154° (*c* 1.7, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 5.381 (d, 1 H, $J_{1,2}$ = 0.4 Hz, H-1), 4.171 (dd, 1 H, $J_{2,3}$ = 5.6 Hz, H-2), 4.050 (dd, 1 H, $J_{3,4}$ = 7.6 Hz, H-3), 3.929 (dq, 1 H, $J_{4,5}$ = 9.7 Hz, H-5), 3.439 (ddd, 1 H, H-4), 3.703 (d, 1 H, $J_{H\text{-}4,OH}$ = 4.0 Hz, HO-4), 2.129 (s, 3 H, SCH_3), 1.538, 1.353 (2 s, 2 × 3 H, $C(CH_3)_2$), 1.304 (d, 3 H, $J_{5,6}$ = 6.2 Hz, H-6); ^{13}C NMR ($CDCl_3$) δ 109.6 ($C(CH_3)_2$), 81.1 (C-1), 78.4 (C-3), 76.6 (C-2), 75.2 (C-4), 65.9 (C-5), 28.1, 26.3 [$(CH_3)_2C$], 17.3 (C-6), 13.3 (SCH_3). Anal. Calcd for $C_{10}H_{18}O_4S$ (234.30): C, 51.26; H, 7.74; S, 13.68. Found: C, 51.08; H, 7.82; S, 13.53.

Methyl 4-*O*-Benzyl-2,3-*O*-isopropylidene-1-thio-α-L-rhamnopyranoside (19). A stirred solution of compound **18** (28 g, 119.5 mmol) in 150 mL of dry DMF was treated with 10 g of sodium hydride (50% dispersion in oil, 208 mmol). The mixture was stirred for 1 h, cooled to 10 °C, and treated dropwise with benzyl bromide (15 mL, 21.6 g, 126 mmol), followed by stirring at 10 °C for 2 h. Excess reagent was decomposed by dropwise addition of 20 mL of methanol. The solution was partitioned between chloroform and water, and the organic layer was dried (Na_2SO_4) and concentrated. Distillation of the residue gave product **19** (37.2 g, 96%), which crystallized spontaneously: mp 53–55 °C; $[\alpha]_D$ −140° (*c* 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.25–7.38 (m, 5 H, aromatic protons), 5.358 (s, 1 H, H-1), 4.902, 4.628 (2 d, 2 × 1 H, *J* = 11.6 Hz, [CH_2 (Bn)]), 4.248 (dd, 1 H, $J_{2,3}$ = 5.7 Hz, $J_{3,4}$ = 7.2 Hz, H-3), 4.172 (d, 1 H, H-2), 3.985 (dq, 1 H, H-5), 3.275 (dd, 1 H, $J_{4,5}$ = 9.8 Hz, H-4), 2.105 (s, 3 H, SCH_3), 1.513, 1.360 (2 s, 2 × 3 H, $C(CH_3)_2$), 1.289 (d, 1 H, $J_{5,6}$ = 6.3 Hz, H-6); ^{13}C NMR ($CDCl_3$) δ 138.3 (aromatic quaternary carbon), 128.3–127.6 (aromatic carbons), 109.3 ($C(CH_3)_2$), 81.6 (C-4), 81.2 (C-1), 78.4 (C-3), 76.8 (C-2), 73.1 [CH_2 (Bn)], 65.2 (C-5), 28.0, 26.4 ($C(CH_3)_2$), 17.9 (C-6), 13.3 (SCH_3). Anal. Calcd for $C_{17}H_{24}O_4S$ (324.42): C, 62.93; H, 7.45; S, 9.88. Found: C, 62.82; H, 7.57; S, 9.69.

Methyl 4-*O*-Benzyl-1-thio-α-L-rhamnopyranoside (20). A solution of isopropylidene derivative **19** (37 g, 114 mmol) in 300 mL of methanol and 20 mL of trifluoroacetic acid was kept at 50 °C for 2 h. The solution was then concentrated, and the residue was triturated with water and hexane. Filtration gave crystalline **20** (26.8 g, 86.4%): mp 79–81 °C; $[\alpha]_D$ −179° (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.4–7.3 (m, 5 H, aromatic protons), 5.108 (d, 1 H, $J_{1,2}$ = 1.5 Hz, H-1), 4.735 [s, 2 H, CH_2 (Bn)], 4.052 (dq, 1 H, H-5), 4.014 (dd, 1 H, $J_{2,3}$ = 3.5 Hz, H-2), 3.882 (dd, 1 H, $J_{3,4}$ = 9.1 Hz, H-3), 3.387 (t, 1 H, $J_{4,5}$ = 9.2 Hz), 2.112 (s, 3 H, SCH_3), 1.361 (d, 1 H, $J_{5,6}$ = 6.3 Hz, H-6); ^{13}C NMR ($CDCl_3$) δ 138.1 (aromatic quaternary carbon), 128.4, 127.7 (aromatic carbons), 85.2 (C-1), 81.6 (C-4), 74.7 [CH_2 (Bn)], 72.3 (C-2), 71.8 (C-3), 67.6 (C-5), 17.8 (C-6), 13.4 (SCH_3). Anal. Calcd for $C_{14}H_{20}O_4S$ (284.36): C, 59.13; H, 7.09; S, 12.68. Found: C, 59.11; H, 7.08; S, 12.80.

Methyl 3,4-Di-*O*-benzyl-1-thio-α-L-rhamnopyranoside (21). A mixture of diol **20** (12 g, 44.7 mmol), dibutyltin oxide (13 g, 52.2 mmol), and 200 mL of dry benzene was stirred under reflux, using a Dean–Stark trap, for 5 h. Benzene (100 mL) was distilled off, and the solution was cooled to ca. 50 °C and treated with tetrabutylammonium bromide (15 g, 46.5 mmol) and benzyl bromide (6.5 mL, 9.4 g, 55 mmol). After the mixture was stirred for 3 h at 50 °C, the solution was concentrated. The residue was stirred with 200 mL of ethyl acetate at 0 °C for 4 h. The solids were removed by filtration and the filtrate was concentrated. Purification of the residue by chromatography with 1:4 ethyl acetate–hexane as eluant gave syrupy **12** (13.1 g, 78.2%): $[\alpha]_D$ −118° (*c* 2.4, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.37–7.26 (m, 10 H, aromatic protons), 5.159 (d, 1 H, H-1), 4.872, 4.638 [2 d, *J* ~ 11 Hz, CH_2 (Bn)], 4.672 [s, 2 H, CH_2 (Bn)], 4.076 (dd, 1 H, $J_{1,2}$ = 1.4 Hz, $J_{2,3}$ = 3.3 Hz, H-2), 4.037 (dq, 1 H, H-5), 3.812 (dd, 1 H, $J_{3,4}$ = 9.1 Hz, H-3), 3.486 (t, 1 H, $J_{4,5}$ = 9.3 Hz, H-4), 2.100 (s, 3 H, SCH_3), 1.319 (d, 3 H, $J_{5,6}$ = 6.2 Hz, H-6); ^{13}C NMR ($CDCl_3$) δ 138.2, 137.5 (aromatic quaternary carbons), 128.4–127.5 (aromatic carbons), 84.6 (C-1, $J_{C\text{-}1,H\text{-}1}$ = 165 Hz), 80.0 (C-3 + C-4), 75.1, 71.9 [2 CH_2 (Bn)], 69.6 (C-2), 67.7 (C-5), 17.7 (C-6), 13.3 (SCH_3).

Methyl 2-*O*-Acetyl-3,4-di-*O*-benzyl-1-thio-α-L-rhamnopyranoside (22). Thiorhamnoside **21** (10 g, 26.7 mmol) was treated with 20 mL of pyridine and 20 mL of acetic anhydride at 25 °C for 6 h. The solution was concentrated. The residue was dissolved in chloroform and washed successively with 5% hydrochloric acid, water, 5% aqueous $NaHCO_3$, and water. The solution was dried (Na_2SO_4) and concentrated to give syrupy **22** (10.6 g, 95.3%), which crystallized spontaneously after 4 weeks: mp 82–83 °C; $[\alpha]_D$ −78° (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.44–7.25 (aromatic protons), 5.438 (dd, 1 H, $J_{1,2}$ = 1.6 Hz, $J_{2,3}$ = 3.4 Hz, H-2), 5.065 (d, 1 H, H-1), 4.908, 4.677, 4.608, 4.511 [4 d, 4 × 1 H, $J \sim 11$ Hz, 2 CH_2 (Bn)], 4.063 (dq, 1 H, H-5), 3.877 (dd, 1 H, $J_{3,4}$ = 9.2 Hz, H-3), 3.462 (t, 1 H, $J_{4,5}$ = 9.4 Hz, H-4), 2.148 (s, 3 H, CH_3CO), 2.112 (s, 3 H, SCH_3), 1.343 (d, 3 H, $J_{5,6}$ = 6.2 Hz, H-6); ^{13}C NMR ($CDCl_3$) δ 170.1 (CH_3CO), 138.3, 137.6 (aromatic quaternary carbons), 128.2–127.6 (aromatic carbons), 83.6 (C-1, $J_{C\text{-}1,H\text{-}1}$ = 165 Hz), 80.1 (C-4), 78.2 (C-3), 75.2, 71.7 [2 CH_2 (Bn)], 70.4 (C-2), 68.1 (C-5), 20.9 (CH_3CO), 17.9 (C-6), 13.8 (SCH_3). Anal. Calcd for $C_{23}H_{28}O_5S$ (416.51): C, 66.32; H, 6.77; S, 7.69. Found: C, 66.06, H, 6.69; S, 7.60.

1-*O*-(2-*O*-Acetyl-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl)-2,3,4,5,6-penta-*O*-benzyl-D-glucitol (23). A mixture of thiorhamnoside **22** (260 mg, 0.625 mmol), alcohol **10** (300 mg, 0.474 mmol), powdered, 4-Å molecular sieves (1.5 g), and 5 mL of dichloromethane was stirred for 1 h, treated with $NOBF_4$ (76 mg, 0.655 mmol), and further stirred for 1 h at 25 °C. The mixture was filtered and the filter cake was washed with dichloromethane (5 × 5 mL). The filtrate was successively washed with ice-cold, 1% aqueous $NaHCO_3$ (5 mL) and water (5 mL), dried (Na_2SO_4), and concentrated. Chromatography of the residue with 5:1 hexane–diethyl ether and then 3:1 hexane–diethyl ether gave syrupy **23** (322 mg, 67.8%): $[\alpha]_D$ −8.3° (*c* 1.3, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 170.1 (CH_3CO), 138.5 (2×), 138.4, 138.3, 138.2 (2×), 137.8 (aromatic quaternary carbons), 128.2–127.3 (aromatic carbons), 97.5 (C-1_B, $J_{C\text{-}1_B,H\text{-}1_B}$ = 168 Hz), 79.9 (C-4_B), 79.0 (C-3_B), 78.5, 78.3, 78.1, 77.7 (C-2_A,3_A,4_A,5_A), 75.0, 74.5, 73.8, 73.3, 73.2, 71.8, 71.5 [CH_2 (Bn)], 69.3 (C-6_A), 68.7 (C-2_B), 67.8 (C-1_A), 67.6 (C-5_B), 21.0 (CH_3CO), 17.9 (C-6).

2,3,4,5,6-Penta-*O*-benzyl-1-*O*-(3,4-di-*O*-benzyl-α-L-rhamnopyranosyl)-D-glucitol (24). A solution of acetate **23** (1.53 g, 1.53 mmol) in 50 mL of methanol was treated with a catalytic amount of sodium methoxide at 25 °C for 6 h. The solution was neutralized with Dowex 50 (H^+) and then concentrated to give compound **24** as a solid glass: 1.45 g (98.5%); $[\alpha]_D$ −19° (*c* 1.8, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 138.6, 138.5 (2×), 138.3 (3×), 137.8 (aromatic quaternary carbons), 128.4–127.3 (aromatic carbons), 98.9 (C-1_B), 79.9 (C-4_B), 79.7 (C-3_B), 79.1, 78.6 (2×), 78.2 (C-2_A,3_A,4_A,5_A), 75.1, 74.6, 73.9, 73.2 (2×), 71.9 (2×) [CH_2 (Bn)], 69.5 (C-6_A), 68.4 (C-2_B), 67.5 (C-1_A), 67.4 (C-5_B), 17.9 (C-6_B).

1-*O*-[2-*O*-(2-*O*-Acetyl-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl]-2,3,4,5,6-penta-*O*-benzyl-D-glucitol (25). A mixture of thiorhamnoside **22** (200 mg, 0.48 mmol), disaccharide **24** (260 mg, 0.27 mmol), powdered, 4-Å molecular sieves (500 mg), and 5 mL of dichloromethane was stirred for 1 h at 25 °C and then treated with $NOBF_4$ (58 mg, 0.5 mmol) at 25 °C for 1 h. The mixture was diluted with dichloromethane and was filtered. The filtrate was washed with 1% aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. The residue was chromatographed with 3:1 hexane–diethyl ether as eluant to give syrupy **25** (225 mg 62.5%): $[\alpha]_D$ −13° (*c* 0.8, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 169.8 (CH_3CO), 138.5–137.9 (aromatic quaternary carbons), 128.3–127.1 (aromatic carbons), 99.1 (C-1_B, $J_{C\text{-}1_B,H\text{-}1_B}$ = 168 Hz), 98.6 (C-1_C, $J_{C\text{-}1_C,H\text{-}1_C}$ = 171 Hz), 79.9, 79.8 (C-4_B,4_C), 79.4, 79.0 (C-3_B,3_C), 78.6, 78.5, 78.2, 77.5 (C-2_A,3_A,4_A,5_A), 74.5 (C-2_B), 75.2, 74.9, 74.5, 73.8, 73.1 (2×), 71.8, 71.7, 71.6 [CH_2 (Bn)], 69.4 (C-6_A), 68.8 (C-2_C), 68.1, 67.9 (C-5_B,5_C), 67.3 (C-1_A), 20.9 (CH_3CO), 17.95, 17.88 (C-6_B,6_C).

2,3,4,5,6-Penta-*O*-benzyl-1-*O*-[3,4-di-*O*-benzyl-2-*O*-(3,4-di-*O*-benzyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl]-D-glucitol (26). Transesterification (Zemplén) of compound **25** as described for compound **23** gave syrupy alcohol **26** in 92.5%: $[\alpha]_D$ −20° (*c* 0.25, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 138.6, 138.5, 138.4, 138.35, 138.30, 138.2 (2×), 138.1, 137.9 (aromatic quaternary carbons), 128.4–127.3 (aromatic carbons), 100.6, 98.7 (C-1_B,1_C), 80.2, 80.0 (C-4_B,4_C), 79.4 (2×) (C-3_B,3_C), 79.0, 78.6, 78.5, 78.2 (C-2_A,3_A,4_A,5_A), 74.6 (C-2_B), 75.2, 75.0, 74.5, 73.8, 73.2, 73.1, 72.0 (2×), 71.8 [CH_2 (Bn)], 69.4 (C-6_A), 68.6 (C-2_C), 67.9, 67.8 (C-5_B,5_C), 67.5 (C-1_A), 18.0, 17.8 (C-6_B,6_C).

Methyl 2,3,4-Tri-*O*-benzoyl-1-thio-α-L-rhamnopyranoside (27). A solution of triol **14** (1.0 g, 5.15 mmol) in 15 mL of pyridine was treated at 0 °C with 3.25 mL (28.06 mmol) of benzoyl chloride. The solution was then allowed to reach 25 °C in 1 h and then was kept standing at 25 °C for 5 h. The mixture was concentrated and the residue was treated with ice water for 2 h. The syrupy residue was dissolved in 20 mL of chloroform, and the solution was successively extracted with 5% aqueous HCl, water, 5% aqueous $NaHCO_3$, and H_2O, dried (Na_2SO_4), and concentrated. Chromatography of the residue with 1:1 ethyl acetate–hexane as eluant gave crystalline **27** (2.34 g, 90%): mp 97–99 °C; $[\alpha]_D$ +111° (*c* 1.1, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 165.7, 165.5, 165.4 (COC_6H_5), 133.4, 133.3, 133.1, 129.9, 129.7, 129.6, 129.4, 129.2, 129.0, 128.5, 128.4, 128.2 (aromatic carbons), 83.5 (C-1), 72.2, 70.3 (C-2,3), 71.9 (C-4), 67.2 (C-5), 17.6 (C-6), 13.9 (SCH_3). Anal. Calcd for $C_{28}H_{26}O_7S$ (506.55): C, 66.38; H, 5.17; S, 6.33. Found: C, 66.19; H, 5.03; S, 6.17.

2,3,4-Tri-*O*-benzoyl-α-L-rhamnopyranosyl Bromide (28). A solution of thiorhamnoside **27** (500 mg, 0.99 mmol) in 10 mL of dichloromethane was treated with bromine (53 μL, 164 mg, 1.0 mmol) at 0 °C for 15 min. The solution was then successively extracted with ice-cold, 1% aqueous $NaHSO_3$ and water, dried (Na_2SO_4), and concentrated. Trituration of the residue with hexane gave crystalline **28** (502 mg, 94.4%): mp 169–171 °C; $[\alpha]_D$ +64° (*c* 1, $CHCl_3$) (lit.[24] mp 163–164 °C; lit.[24] $[\alpha]_D$ +64.8 (*c* 1.44, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 8.13–7.19 (m, 15 H, aromatic protons), 6.560 (dd, 1 H, $J_{1,2}$ = 1.7 Hz, $J_{1,5}$ = 0.7 Hz, H-1), 6.214 (dd, 1 H, $J_{2,3}$ = 3.4 Hz, $J_{3,4}$ = 10.3 Hz, H-3), 5.888 (dd, 1 H, H-2), 5.787 (t, 1 H, $J_{4,5}$ = 10.0 Hz, H-4), 4.439 (ddq, 1 H, H-5), 1.430 (d, 3 H, $J_{5,6}$ = 6.3 Hz, H-6); ^{13}C NMR ($CDCl_3$) δ 165.5, 165.2, 165.0 (CO-C_6H_5), 133.6–128.1 (aromatic carbons), 83.8 (C-1, $J_{C\text{-}1,H\text{-}1}$ = 196 Hz), 73.3 (C-2), 71.4 (C-5), 70.9 (C-4), 68.8 (C-3), 17.1 (C-6). Anal. Calcd for $C_{27}H_{23}BrO_7$ (539.36): C, 60.12; H, 4.29; Br, 14.82. Found: C, 59.62; H, 4.14; Br, 14.56.

1-*O*-{2-*O*-[2-*O*-(2,3,4-Tri-*O*-benzoyl-α-L-rhamnopyranosyl)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl]-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl}-2,3,4,5,6-penta-*O*-benzyl-D-glucitol (29). A mixture of trisaccharide **26** (155 mg, 0.12 mmol), *N,N,N′,N′*-tetramethylurea (36 μL, 0.30 mmol), silver trifluoromethanesulfonate (140 mg, 0.55 mmol), 4-Å molecular sieves (300 mg), and dichloromethane (5 mL) was stirred at 25 °C for 1 h, cooled to −60 °C, and treated with a solution of bromide **28** [prepared from thiorhamnoside **27** (150 mg, 0.3 mmol)] in 3 mL of dichloromethane. Stirring was continued at 25 °C for 12 h. The mixture was treated with tetraethylammonium bromide (~0.3 g) and was filtered. The filtrate was washed with water, dried (Na_2SO_4), and chromatographed with 2:1 hexane–diethyl ether as eluant to give amorphous **29** (140 mg, 66.4%): $[\alpha]_D$ +27° (*c* 0.7, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 165.8, 165.4, 165.2 (COC_6H_5), 138.6–138.0, 133.2–132.9, 129.8–129.2, 128.4–127.3 (aromatic carbons), 100.3 ($^1J_{C,H}$ = 171 Hz), 99.2 ($^1J_{C,H}$ = 168 Hz), 98.8 ($^1J_{C,H}$ = 170 Hz) (C-1_B,1_C,1_D), 80.4, 80.2 (C-4_B,4_C), 79.6 (C-3_B), 79.1 (2×), 78.8, 78.6, 78.3 (C-3_C, C-2_A,3_A,4_A,5_A), 76.0 (C-2_B), 74.5 (C-2_C), 75.5, 75.1, 74.6, 73.9, 73.3, 73.2, 72.5, 72.3, 71.9 [CH_2 (Bn)], 71.9 (C-4_D), 70.7 (C-3_D), 69.6 (C-2_D), 68.7, 68.1, 67.1 (C-5_B,5_C,5_D), 18.0 (2×), 17.5 (C-6_B,6_C,6_D).

2-*O*-Acetyl-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl Bromide (30). A solution of thiorhamnoside **22** (128 mg, 0.307 mmol) in 4 mL of dichloromethane was treated with bromine (16 μL, 49.6 mg, 0.31 mmol) at 0 °C for 15 min. Workup (as given for compound **28**) provided syrupy **30** [137 mg (100%)]: $[\alpha]_D$ −108° (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.36–7.14 (m, 10 H, aromatic protons), 6.300 (d, 1 H, $J_{1,2}$ = 1.6 Hz, H-1), 5.515 (dd, 1 H, $J_{2,3}$ = 3.4 Hz, H-2), 4.92, 4.68, 4.63, 4.56 [4 d, $J \sim 11$ Hz, 2 CH_2 (Bn)], 4.324 (dd, 1 H, $J_{3,4}$ = 9.4 Hz, H-3), 3.959 (ddq, 1 H, $J_{1,5}$ = 0.7 Hz, H-5), 3.504 (t, 1 H, $J_{4,5}$ = 9.5 Hz, H-4), 2.141 (s, 3 H, CH_3CO), 1.355 (d, 1 H, $J_{5,6}$ = 6.3 Hz, H-6); ^{13}C NMR ($CDCl_3$) δ 169.7 ($COCH_3$), 138.0, 137.4 (quaternary aromatic carbons), 128.3–127.7 (aromatic carbons), 85.7 (C-1, $J_{C\text{-}1,H\text{-}1}$ = 185 Hz), 79.1 (C-4), 77.7 (C-3), 75.4, 71.9 [CH_2 (Bn)], 72.5 (C-5), 71.7 (C-2), 20.8 (CH_3CO), 17.3 (C-6).

Methyl 2-*O*-Benzoyl-3,4-di-*O*-benzyl-1-thio-α-L-rhamnopyranoside (32). A solution of thiorhamnoside **21** (1.5 g, 4.0 mmol) in 10 mL of pyridine was treated with 0.7 mL (848 mg,

6.0 mmol) of benzoyl chloride at 0 °C for 12 h. Usual workup (as described for compound **27**) followed by chromatography with 9:1 hexane–diethyl ether gave syrupy **32** (1.72 g, 89.8%): $[\alpha]_D$ −26° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz) δ 8.21–8.04, 7.72–7.19 (m, 15 H, aromatic protons), 5.674 (dd, 1 H, $J_{2,3}$ = 3.3 Hz, H-2), 5.203 (d, 1 H, $J_{1,2}$ = 1.7 Hz, H-1), 4.91, 4.75, 4.64, 4.55 [4 d, $J \sim 11$ Hz, 2 CH_2 (Bn)], 4.111 (dq, 1 H, H-5), 3.990 (dd, 1 H, $J_{3,4}$ = 9.2 Hz, H-3), 3.577 (t, 1 H, $J_{4,5}$ = 9.3 Hz, H-4), 2.141 (s, 3 H, SCH_3), 1.373 (d, 1 H, $J_{5,6}$ = 6.2 Hz, H-6); ^{13}C NMR ($CDCl_3$) δ 165.7 (COC_6H_5), 138.4, 137.8 [aromatic quaternary carbons (Bn)], 133.2–127.6 (aromatic carbons), 83.8 (C-1), 80.2 (C-4), 78.5 (C-3), 75.3, 71.6 [CH_2 (Bn)], 71.1 (C-2), 68.3 (C-5), 18.1 (C-6), 13.9 (SCH_3).

Methyl 2-*O*-(2-*O*-Benzoyl-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl)-3,4-di-*O*-benzyl-1-thio-α-L-rhamnopyranoside (34). A solution of benzoate **32** (1.72 g, 3.59 mmol) in 10 mL of dichloromethane was treated with bromine (185 μL, 3.59 mmol) at 0 °C for 20 min and then concentrated. Toluene (5 mL) was added and the solution was concentrated to a syrup (**33**), a solution of which in 10 mL of dichloromethane was added to a mixture of thiorhamnoside **21** (1.25 g, 3.34 mmol), *N,N,N',N'*-tetramethylurea (900 μL, 874 mg, 7.5 mmol), 4-Å molecular sieves (2 g), and 10 mL of dichloromethane, previously stirred at 25 °C for 1 h. The combined mixture was further stirred at 25 °C for 1 h, cooled to −60 °C, and treated with silver trifluoromethanesulfonate (0.92 g, 3.59 mmol). Stirring was continued at −20 °C for 1 h and then at 0 °C for 1 h. Tetraethylammonium bromide (1 g) was added, and the mixture was filtered. Concentration of the filtrate gave a syrup, chromatography of which with 4:1 hexane–diethyl ether as eluant gave syrupy **34** (1.52 g, 53.9%): $[\alpha]_D$ −32° (*c* 0.6, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 165.4 (COC_6H_5), 138.4, 138.3, 137.9 (2×) [quaternary aromatic carbons (Bn)], 133.0, 130.0–127.5 (aromatic carbons), 99.3 ($C\text{-}1_B$, $J_{C\text{-}1_B,H\text{-}1_B}$ = 172 Hz), 84.8 ($C\text{-}1_A$, $J_{C\text{-}1_A,H\text{-}1_A}$ = 168 Hz), 80.12, 80.08, 80.0 ($C\text{-}3_A,4_A,4_B$), 77.7 ($C\text{-}3_B$), 76.3 ($C\text{-}2_A$), 75.3, 75.2, 72.2, 71.5 [CH_2 (Bn)], 69.3 ($C\text{-}2_B$), 68.4, 68.3 ($C\text{-}5_A,5_B$), 18.1, 17.9 ($C\text{-}6_A,6_B$), 13.7 (SCH_3).

Methyl 2-*O*-{2-*O*-[2-*O*-Benzoyl-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl]-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl}-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (36). A mixture of disaccharide **34** (240 mg, 0.296 mmol), acceptor **35**[7] (210 mg, 0.586 mmol), 4-Å molecular sieves (~0.4 g), and 8 mL of dichloromethane was stirred at 25 °C for 2 h and then treated with nitrosyl tetrafluoroborate (36 mg, 0.3 mmol) for 2 h at 25 °C. The mixture was filtered. The filtrate was washed with 1% aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. Chromatography of the residue with 1:1 hexane-diethyl ether as eluant gave syrupy **36** (119 mg, 36%): $[\alpha]_D$ −54° (*c* 0.7, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 165.5 (COC_6H_5), 138.4, 138.2 (aromatic quaternary carbons), 133.0, 130.2–127.7 (aromatic carbons), 100.3 ($^1J_{C,H}$ = 171 Hz), 99.9 ($^1J_{C,H}$ = 169 Hz), 99.2 ($^1J_{C,H}$ = 171 Hz) ($C\text{-}1_A,1_B,1_C$), 80.25, 80.15 (2×) ($C\text{-}4_A,4_B,4_C$), 79.6, 79.0 ($C\text{-}3_A,3_B$), 77.9 ($C\text{-}3_C$), 75.2, 74.3 ($C\text{-}2_A,2_B$), 75.32, 75.22 (2×), 72.2, 72.0, 71.5 [CH_2 (Bn)], 69.5 ($C\text{-}2_C$), 68.4, 68.3, 67.7 ($C\text{-}5_A,5_B,5_C$), 54.5 (OCH_3), 18.0 (3×) ($C\text{-}6_A,6_B,6_C$).

1-*O*-[2-*O*-(2-*O*-Benzoyl-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl]-2,3,4,5,6-penta-*O*-benzyl-D-glucitol (37) and 1-*O*-[2-*O*-(2-*O*-Benzoyl-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl)-3,4-di-*O*-benzyl-β-L-rhamnopyranosyl]-2,3,4,5,6-penta-*O*-benzyl-D-glucitol (38). A mixture of disaccharide **34** (400 mg, 0.49 mmol), alcohol **10** (600 mg, 0.95 mmol), 4-Å molecular sieves (~0.5 g), and 15 mL of dichloromethane was stirred at 25 °C for 3 h, cooled to 0 °C, and treated with nitrosyl tetrafluoroborate (58 mg, 0.5 mmol). The stirred mixture was allowed to reach 25 °C, stirred for a further 2.5 h, and filtered. The filtrate was extracted with water, dried (Na_2SO_4), and concentrated. Chromatography of the residue with 3:1 hexane–diethyl ether gave syrupy **37** (290 mg, 42%): $[\alpha]_D$ +16° (*c* 1.2, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 165.4 (COC_6H_5, 138.63, 138.59, 138.5, 138.4, 138.35, 138.25 (2×), 138.2, 138.0 (aromatic quaternary carbons), 132.3, 130.0, 129.8, 128.3–127.3 (aromatic carbons), 99.3 ($^1J_{C,H}$ = 168 Hz), 98.6 ($^1J_{C,H}$ = 170 Hz) ($C\text{-}1_B,1_C$), 80.1, 80.0 ($C\text{-}4_B,4_C$), 79.5, 79.1 ($C\text{-}3_B,3_C$), 78.7, 78.6, 78.3, 77.6 ($C\text{-}2_A,3_A,4_A,5_A$), 74.9 ($C\text{-}2_B$), 75.3, 75.0, 74.6, 73.9, 73.24, 73.19, 72.0, 71.9, 71.5 [CH_2 (Bn)], 69.5 ($C\text{-}6_A$), 69.4 ($C\text{-}2_C$), 68.2, 68.0 ($C\text{-}5_B,5_C$), 67.5 ($C\text{-}1_A$), 18.1, 18.0 ($C\text{-}6_B,6_C$).

Further elution gave syrupy **38** (118 mg, 17%): $[\alpha]_D$ 0° (*c* 1.4, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 165.5 (COC_6H_5), 138.9, 138.7 (2×), 138.6, 138.33 (2×), 138.28, 138.2, 137.7 (aromatic quaternary carbons), 132.9, 130.2, 129.8, 128.3–127.3 (aromatic carbons), 100.5 ($C\text{-}1_B$, $J_{C\text{-}1_B,H\text{-}1_B}$ = 155 Hz), 98.2 ($C\text{-}1_C$, $J_{C\text{-}1_C,H\text{-}1_C}$ = 173 Hz), 82.7, 80.1, 79.7, 79.0, 78.9, 78.6 (2×), 78.1 ($C\text{-}2_A,3_A,4_A,5_A$, $C\text{-}3_B$, $C\text{-}3_C$, $C\text{-}4_B$, $C\text{-}4_C$), 75.3, 75.0, 74.0, 73.9, 73.3, 73.2, 71.85, 71.79, 71.5, 71.4 [$C\text{-}1_A$, CH_2 (Bn)], 72.2, 71.7 ($C\text{-}2_B,2_C$), 69.62 ($C\text{-}6_A$), 69.56, 67.67 ($C\text{-}5_B,5_C$).

Methyl 2,3,4,6-Tetra-*O*-acetyl-1-thio-α-L-mannopyranoside (40) and Methyl 2,3,4,6-Tetra-*O*-acetyl-1-thio-β-L-mannopyranoside (41). A solution of L-mannose (3 g, 16.6 mmol) in 15 mL of pyridine was treated with 15 mL of acetic anhydride at 5 °C for 10 h. The solution was concentrated. The residue was treated with ice water for 1 h and chloroform was added. The resulting solution was successively extracted with 5% aqueous HCl, water, 5% aqueous $NaHCO_3$, and water, dried (Na_2SO_4), and concentrated to give syrupy **39** (6.2 g, 96%) as a ca. 85:15 mixture of the α and β anomers [^1H NMR ($CDCl_3$) δ 6.081 (H-1α, $J_{1,2}$ = 1.6 Hz), 5.861 (H-1β, $J_{1,2}$ = 1.2 Hz).

A mixture of pentaacetate **39** (2 g, 5.12 mmol), $CH_3SSi(CH_3)_3$ (3 g, 3.54 mL, 25 mmol), 4-Å molecular sieves (~2 g), and 20 mL of dichloromethane was stirred for 1 h at 25 °C. Trimethylsilyl trifluoromethanesulfonate (2.3 g, 2 mL, 10.3 mmol) was then added, and the mixture was further stirred for 36 h, diluted with 50 mL of dichloromethane, and filtered. The filtrate was washed with ice-cold, 5% aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. Chromatography of the residue with 3:2 hexane–ethyl acetate gave first crystalline **40** (1.3 g, 67%): mp 123–125 °C; $[\alpha]_D$ −99° (*c* 1.7, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 5.353 (dd, 1 H, $J_{1,2}$ = 1.6 Hz, $J_{2,3}$ = 3.1 Hz, H-2), 5.31 (m, H-4), 5.283 (dd, 1 H, $J_{3,4}$ = 9.9 Hz, H-3), 5.174 (d, 1 H, H-1), 4.34 (m, H-5), 4.323 (dd, 1 H, $J_{5,6}$ = 5.3 Hz, $J_{6,6'}$ = 12 Hz, H-6), 4.130 (dd, 1 H, $J_{5,6'}$ = 2.0 Hz, H-6'), 2.165, 2.153, 2.103, 2.054, 1.993 (5 s, 5 × 3 H, SCH_3, 4 CH_3CO); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.5, 169.9, 169.74, 169.67 ($CO\text{-}CH_3$), 83.5 (C-1, $J_{C\text{-}1,H\text{-}1}$ = 168 Hz), 70.7 (C-2), 69.4 (C-3), 68.8 (C-5), 66.3 (C-4), 62.4 (C-6), 20.85, 20.68, 20.64, 20.57 (CH_3CO), 13.6 (SCH_3). Anal. Calcd for $C_{15}H_{22}O_9S$ (378.39): C, 47.61; H, 5.86; S, 8.47. Found: C, 47.91; H, 5.94; S, 8.33.

Further elution gave a mixture of **40** and **41** (240 mg, 12.4%).

Subsequent elution afforded crystalline **41** (230 mg, 12%): mp 180–183 °C; $[\alpha]_D$ +43° (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 5.520 (dd, 1 H, $J_{1,2}$ = 1.2 Hz, $J_{2,3}$ = 3.5 Hz, H-2), 5.279 (t, 1 H, $J_{4,5}$ = 10 Hz, H-4), 5.070 (dd, 1 H, $H_{3,4}$ = 10.1 Hz, H-3), 4.292 (dd, 1 H, $J_{5,6}$ = 5.2 Hz, $J_{6,6'}$ = 12.3 Hz, H-6), 4.155 (dd, 1 H, $J_{5,6'}$ = 2.5 Hz, H-6'), 3.698 (dq, 1 H, H-5), 2.262 (s, 3 H, SCH_3), 2.190, 2.087, 2.046, 1.984 (4 s, 4 × 3 H, 4 CH_3CO); ^{13}C NMR ($CDCl_3$) δ 170.5, 170.0, 169.8, 169.4 ($COCH_3$), 83.5 (C-1, $J_{C\text{-}1,H\text{-}1}$ = 153 Hz), 76.3 (C-5), 71.7 (C-3), 70.0 (C-2), 65.7 (C-4), 62.6 (C-6), 20.5 (CH_3CO), 14.1 (SCH_3). Anal. Calcd for $C_{15}H_{22}O_9S$ (378.39): C, 47.61; H, 5.86; S, 8.47. Found: C, 47.90, H, 5.93; S, 8.31.

Methyl 2-*O*-(2,3,4,6-Tetra-*O*-acetyl-α-L-mannopyranosyl)-3,4-di-*O*-benzyl-1-thio-α-L-rhamnopyranoside (43). A solution of thiomannoside **40** (600 mg, 1.58 mmol) in 6 mL of dichloromethane was treated with bromine (99 μL, 307 mg, 1.92 mmol) at 0 °C. The solution was allowed to reach 20 °C in 20 min an then was concentrated. Toluene (2 × 5 mL) was added to and evaporated from the syrupy residue. Subsequently, the residue was treated with 10 mL of dichloromethane, and the resulting solution was added to a stirred mixture of thiorhamnoside **21** (500 mg, 1.33 mmol), 4-Å molecular sieves (~1.5 g), *N,N,N',N'*-tetramethylurea (195 μL, 1.64 mmol), silver trifluoromethanesulfonate (410 mg, 1.60 mmol), and 10 mL of dichloromethane at −40 °C. The mixture was allowed to reach 25 °C in ca. 30 min, stirred at 25 °C for a further 2 h, treated with tetraethylammonium bromide (~0.5 g), and filtered. The filtrate was concentrated and the residue was chromatographed with 7:3 hexane–ethyl acetate as eluant to give syrupy **43** (395 mg, 42%): $[\alpha]_D$ −87° (*c* 0.8, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 170.1, 169.4 (2×), 169.2 ($COCH_3$), 138.1, 137.7 (aromatic quaternary carbons), 128.0–127.3 (aromatic carbons), 98.9 ($C\text{-}1_B$, $J_{C\text{-}1_B,H\text{-}1_B}$ = 173 Hz), 84.2 ($C\text{-}1_A$, $J_{C\text{-}1_A,H\text{-}1_A}$ = 166 Hz), 79.9 ($C\text{-}4_A$), 79.5 ($C\text{-}3_A$), 77.3 ($C\text{-}2_A$), 75.0, 72.1 [CH_2 (Bn)], 69.0, 68.7 (2×), 68.2, 66.0 ($C\text{-}5_A$, $C\text{-}2_B,3_B,4_B,5_B$), 62.3 ($C\text{-}6_B$), 20.4, 20.3 (3×) (CH_3CO), 17.6 ($C\text{-}6_A$), 13.4 (SCH_3).

Methyl 2-*O*-[2-*O*-(2,3,4,6-Tetra-*O*-acetyl-α-L-mannopyranosyl)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl]-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (44). A mixture of disaccharide

43 (470 mg, 0.667 mmol), alcohol 35[7] (310 mg, 0.866 mmol), 4-Å molecular sieves (~0.8 g), and 10 mL of dichloromethane was stirred for 1 h at 25 °C and then treated with nitrosyl tetrafluoroborate (80 mg, 0.689 mmol). The mixture was stirred for a further 2 h and then filtered. The filtrate was extracted with 1% aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. Chromatography of the residue gave syrupy **44** (230 mg, 34%): $[\alpha]_D$ −28° (*c* 1, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 170.3, 169.7, 169.5 (2×) ($COCH_3$), 138.4, 138.3, 138.2, 138.1 (aromatic quaternary carbons), 128.4–127.3 (aromatic carbons), 99.8 (2×) ($^1J_{C,H}$ = 170 Hz), 99.1 ($^1J_{C,H}$ = 171 Hz) (C-1_A,1_B,1_C), 80.3, 80.1 (C-4_A,4_B), 79.7, 78.8 (C-3_A,3_B), 76.6, 74.2 (C-2_A,2_B), 75.3, 75.1, 72.3, 72.2 [CH_2 (Bn)], 69.4, 69.0, 68.8, 68.6, 67.6, 65.9 (C-5_A,5_B, C-2_C,3_C,4_C,5_C), 62.0 (C-6_C), 54.4 (OCH_3), 20.7, 20.5 (3×) (CH_3CO), 17.9 (2×) (C-6_A,6_B).

Methyl 2-*O*-(2,3,4,6-Tetra-*O*-acetyl-α-L-mannopyranosyl)-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (45). A mixture of thiomannoside **40** (230 mg, 0.608 mmol), alcohol **35**[7] (265 mg, 0.739 mmol), 4-Å molecular sieves (~1 g), and 8 mL of dichloromethane was stirred for 1 h at 25 °C and then treated with nitrosyl tetrafluoroborate (75 mg, 0.646 mmol). After stirring for 1.5 h at 25 °C, the mixture was filtered, and the filtrate was treated with 3 mL of pyridine and 3 mL of acetic anhydride for 12 h at 25 °C. Removal of solvents left a syrup, which was chromatographed with 4:1 hexane–ethyl acetate as eluant to give first methyl 2-*O*-acetyl-3,4-di-*O*-benzyl-α-L-rhamnopyranoside[7] (83 mg). Further elution gave unidentified products (~100 mg) followed by syrupy **45** (215 mg, 51.4%): $[\alpha]_D$ −30° (*c* 0.5, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 170.4, 169.7 (2×) 169.5 ($COCH_3$), 138.3, 138.1 (aromatic quaternary carbons), 128.2–127.2 (aromatic carbons), 99.4 ($^1J_{C,H}$ = 172 Hz), 99.2 ($^1J_{C,H}$ = 169 Hz) (C-1_A,1_B), 80.4 (C-4_A), 79.4 (C-3_A), 76.0 (C-2_A), 75.3, 72.2 [CH_2 (Bn)], 69.2, 68.9, 68.8, 67.8, 66.1 (C-5_A, C-2_B,3_B,4_B,5_B), 62.5 (C-6_B), 54.4 (OCH_3), 20.6, 20.5 (3×) (CH_3CO), 17.8 (C-6_A).

1-*O*-{2-*O*-[2-*O*-(α-L-Rhamnopyranosyl)-α-L-rhamnopyranosyl]-α-L-rhamnopyranosyl}-D-glucitol (2). A solution of compound **29** (120 mg, 0.068 mmol) in 5 mL of methanol was treated with sodium methoxide until the pH of the solution reached ~11 (indicator paper); then the solution was left standing at 25 °C for 24 h. The solution was neutralized (Dowex 50, H^+) and concentrated. A mixture of the residue and 10% palladium on carbon (~200 mg) in 95% ethanol (5 mL) and glacial acetic acid (1 mL) was stirred under hydrogen (1 atm) for 24 h at 25 °C. Removal of the catalyst by filtration followed by concentration gave a syrupy residue, which was purified through a column of Sephadex G-15 eluted with water. Freeze-drying of the major fraction gave **2** as an amorphous white powder (28 mg, 66.6%); $[\alpha]_D$ −52° (*c* 3.2, H_2O). For ^1H and ^{13}C NMR data, see Tables I and II, respectively.

1-*O*-(α-L-Rhamnopyranosyl)-D-glucitol (3). Deprotection of compound **23** as described for the deprotection of **29**, except that a Sephadex G-10 column was used for the final purification, gave amorphous **3** (73%); $[\alpha]_D$ −37° (*c* 1.7, H_2O). For ^1H and ^{13}C NMR data, see Tables I and II, respectively.

Methyl 2-*O*-(α-L-Mannopyranosyl)-α-L-rhamnopyranoside (4). Deprotection of compound **45** as described for compound **23** afforded amorphous **4** (75%); $[\alpha]_D$ −49° (*c* 0.4, H_2O) [lit.[41] $[\alpha]_D$ −54° (*c* 1, H_2O)]. For ^1H and ^{13}C NMR data, see Tables I and II, respectively.

1-*O*-[2-*O*-(α-L-Rhamnopyranosyl)-α-L-rhamnopyranosyl]-D-glucitol (5). Deprotection of compound **25** as described for compound **29** gave **5** as an amorphous powder (65%); $[\alpha]_D$ −40° (*c* 1.0, H_2O). For ^1H and ^{13}C NMR data, see Tables I and II, respectively.

Methyl 2-*O*-[2-*O*-(α-L-Mannopyranosyl)-α-L-rhamnopyranosyl]-α-L-rhamnopyranoside (6). Removal of protecting groups from compound **44** as described for compound **45** gave amorphous **6** (68%); $[\alpha]_D$ −54° (*c* 1.1, H_2O). For ^1H and ^{13}C NMR data, see Tables I and II, respectively.

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Regiospecific Addition of Monooxygenated Dienes to Halo Quinones

Louise Boisvert and Paul Brassard*

Département de chimie, Université Laval, Québec, Québec, Canada G1K 7P4

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In spite of their decreased polarity with respect to previously studied electron-rich analogues, monooxygenated dienes also react regiospecifically with halo quinones. The corresponding adducts can easily be aromatized on silica gel to isomeric polysubstituted naphthoquinones of unambiguous structure and therefore provide ready access to substrates for subsequent regiospecific annulations. The scope of this approach is illustrated by advantageous syntheses of several natural products: chimaphilin, 6-methylalizarin, 6-methylxanthopurpurin, and barleriaquinone. The adducts can also give rise to a series of products in which the oxygen function of the dienes is preserved as a hydroxyl group in the quinone. To this end adducts derived from 1-oxygenated dienes and halo quinones were oxidized effectively with Jones' reagent while those obtained from the 2-oxygenated isomers responded better to manganese dioxide. Relative positions of substituents in the adducts were readily confirmed by comparison of some of the hydroxylated oxidation products with known compounds of unambiguous structure. The method is again illustrated by the ready synthesis of a number of natural products including plumbagin, soranjidiol, isochrysophanol and its 8-methyl ether, and isozyganein and its 5-methyl ether.

Regioselective annulations of quinones by the Diels–Alder strategy have been described with weakly or moderately polar dienes, appropriately substituted dienophiles, or catalysis by Lewis acids. Various combinations of these factors can produce remarquable effects[1] and highly selective results.[2] However, these approaches depend on structural features that can curtail their applicability and usefulness or, as in the case of catalysis, render the outcome unpredictable.

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