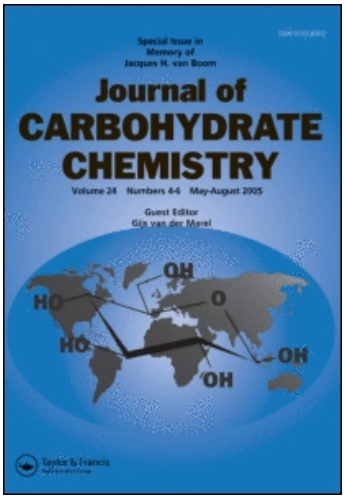

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András Lipták[a]; Lajot Szabó[a]; János Harangi[a]
[a] L. Kossuth University, Institute of Biochemistry, Debrecen, Hungary

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SYNTHESIS OF METHYL 1-THIO-L-RHAMNOPYRANOSIDE DERIVATIVES

András Lipták, Lajos Szabó and János Harangi

L. Kossuth University, Institute of Biochemistry,
P.O.Box 55, H-4010 Debrecen, Hungary

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ABSTRACT

Both anomers of methyl 1-thio-L-rhamnopyranosides were prepared through methylation of the corresponding isothiouronium salt. 2,3-O-Isopropylidene-, benzylidene- and the until now unknown diphenylmethylene acetals were synthesized. Phase-transfer catalysed benzylation and $LiAlH_4$-$AlCl_3$-type hydrogenolysis of benzylidene acetals were used to obtain partially benzylated derivatives. Comparing the ^{13}C NMR data of the synthesized compounds with those of their O-glycoside analogues revealed that the O→S exchanges at the anomeric centres caused drastic upfield shifts (~15 ppm) at C-1 and moderate downfield shifts at C-2 and C-5, as well. The chemical shift values of other carbons are not sensitive to the O→S replacement.

INTRODUCTION

Activation of thioglycosides by methyl triflate using Lönn's method[1] offered a new and very effective method for preparing complex oligosaccharides. The main advantage of this method is that the thioglycosides can be functionalized in desired manners and used as glycosyl donors. At the same time, the partially substituted thioglycosides can also serve as glycosyl acceptors in oligosaccharide synthesis, depending on the type of promotors.[2] For this reason the thioglycosides and their derivatives are very valuable starting materials of synthetic carbohydrate chemistry. In this paper we report the synthesis of some deriv-

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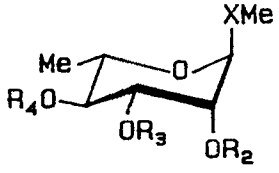
Dedicated to Professor Pál Nánási on the occasion of his 65th birthday.



1 $R_2=R_3=R_4=Ac$

3 $R_2=R_3=R_4=H$

8 $R_2=R_3=H$; $R_4=Bzl$

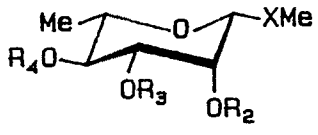
9 $R_2=R_4=Bzl$; $R_3=H$

10 $R_2=H$; $R_3=R_4=Bzl$

11 $R_2=R_4=Bzl$; $R_3=Ac$

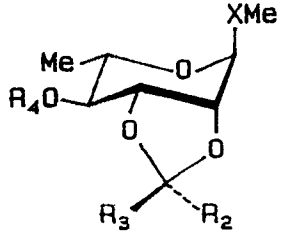
20 $R_2=R_4=H$; $R_3=Bzl$

21 $R_2=Bzl$; $R_3=R_4=H$



2 $R_2=R_3=R_4=Ac$

4 $R_2=R_3=R_4=H$



5 $R_2=R_3=CH_3$; $R_4=H$

7 $R_2=R_3=CH_3$; $R_4=Bzl$

12 $R_2=R_3=Ph$; $R_4=H$

14 $R_2=R_3=Ph$; $R_4=Ac$

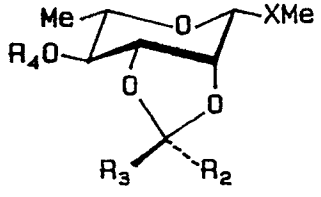
15 $R_2=R_3=Ph$; $R_4=Bzl$

16 $R_2=R_4=H$; $R_3=Ph$

17 $R_3=R_4=H$; $R_2=Ph$

18 $R_2=H$; $R_3=Ph$; $R_4=Ac$

19 $R_2=Ph$; $R_3=H$; $R_4=Ac$



6 $R_2=R_3=CH_3$; $R_4=H$

13 $R_2=R_3=Ph$; $R_4=H$

X = S or O

atives of both anomers of methyl 1-thio-L-rhamnopyranosides and compare the ^{13}C NMR data of these compounds with their O-glycoside congeners.

RESULTS AND DISCUSSION

Acetobromo-L-rhamnose was treated with thiourea and the formed isothiouronium salt was methylated with methyl iodide in the presence of Hünig's base to give methyl 2,3,4-tri-O-acetyl-1-thio-α-L- (1-S) and -β- L-rhamnopyranoside (2-S). Compound 2-S crystallized from the reaction mixture although it represented only 6-8% of the mixture. The α-anomer 1-S[3] was purified by column cromatography but has not been obtained in the crystallized form. Conventional deacetylation of the triacetates resulted in crystalline methyl 1-thio-α-L-(3-S) and -β-L-rhamnopyranoside (4-S). Treatment of compounds 3-S and 4-S with 2,2-dimethoxypropane without solvent[4] or in the presence of traces of N,N-dimethylformamide was done using a toluene-p-sulphonic acid catalyst; the isopropylidene derivatives (5-S and 6-S) were isolated in crystalline forms.

Conventional benzylation of 5-S resulted in the fully protected, crystalline 7-S. The isopropylidene group from compound 7-S was removed by acid hydrolysis to give 8-S which was treated with benzyl bromide under phase-transfer catalytic conditions[5] giving the 2,4-di-O-benzyl ether (9-S) isolated in a yield of 76%. The 3,4-di-O-benzyl isomer (10-S) appeared as a minor component with a yield of 3%. To distinguish between structures 9-S and 10-S, 9-S was acetylated to give 11-S and the location of the acetyl group was verified by ^{1}H NMR spectroscopy.

The anomeric unsubstituted glycosides (3-S and 4-S) were separately treated[6] with diclorodiphenylmethane in pyridine to give the diphenylmethylene acetals (12-S and 13-S). The reactivity of the β-anomer 4-S was extremely low compared to the reactivity of the α-anomer 3-S, and only a very moderate yield of 13-S could be obtained. A similar difference between the reactivity of the two anomers was not observed during the formation of the isopropylidene acetals. The different steric requirement of the phenyl versus methyl groups is a probable explanation. The diphenylmethylene acetal seems to be a very

useful protecting group and it can be removed by mild acid hydrolysis, or by catalytic hydrogenolysis. Chemical reduction with $LiAlH_4$-$AlCl_3$ at low temperature cleaves them into diphenylmethyl ethers,[6] but at higher temperature (~45°C) both OH groups can be regenerated. These properties might find useful applications in preparative carbohydrate chemistry.

It is worth noting that the conventional preparation of acetals, i.e., condensation of benzophenone dimethyl acetal with diols, failed. The later reaction gave methyl 6-O-(methoxydiphenylmethyl)-α-D-glucopyranoside[7] from methyl α-D-glucopyranoside. There is only one other successful approach in the literature, the preparation of 1,2-O-diphenylmethylene acetal of D-ribofuranose dibenzoate using diphenyl cadmium.[8]

Acetylation of 12-S provided 14-S while benzylation gave 15-S. Both are completely protected sugars with three different temporary blocking groups and have rhamnosyl donor ability.

Benzylidenation[9] of 3-S with α,α-dimethoxy-toluene without solvent in presence of a catalytic amount of p-toluenesulphonic acid gave a 1:1 mixture of the exo- (16-S) and endo-phenyl-benzylidene (17-S) derivatives. This reaction requires a very short reaction time, and the yield is also high. The unseparable isomers were acetylated, the 4-O-acetyl isomer (18-S) of 16-S was crystallized from ethanol and the syrup 19-S was purified by column chromatography. Their saponification resulted in compounds 16-S and 17-S. Hydrogenolysis of the dioxolane-type benzylidene derivatives 16-S and 17-S followed the well-known general route,[10] 16-S gave 3-O-benzyl ether (20-S) and compound 17-S gave the 2-O-benzyl derivative (21-S).

The ^{13}C NMR spectra of all new compounds were assigned by using their proton-carbon correlation maps and data were compared with those of the corresponding O-glycoside derivatives. In most cases the ^{13}C NMR spectra of the O-glycosides have already been published. Here we report only the synthesis and ^{13}C NMR data of methyl 2,3-O-diphenylmethylene-α-L-rhamnopyranoside (12-O), its 4-O-acetyl- (14-O) and 4-O-benzyl-derivatives (15-O). Treatment of methyl α-L-rhamnopyranoside[11] with dichlorodiphenylmethane as described for the preparation of 12-S afforded 12-O. Conventional acetylation gave 14-O and benzylation of

^{13}C-NMR chemical shift data (ppm.)
(The assignments are based on proton-carbon correlations.)

		C-1	C-2	C-3	C-4	C-5	C-6	XCH_3	$C(\underline{C}H_3)_2$		C(ac)	$\underline{C}H_2Ph$	
1	O	98.41	69.74	69.04	71.02	66.13	17.30	54.98					
1	S	83.26	71.03	69.34	71.11	66.77	17.28	13.65					
2	O	99.40	68.84	71.05	70.73	70.45	17.28	57.08					
2	S	83.17	70.36	71.75	70.36	74.86	17.45	14.12					
3	O	102.1	71.2	71.5	70.3	69.5	17.9	54.8					
3	S	86.26	71.99	71.14	72.72	69.29	16.94	13.31					
4	O	102.4	71.8	74.1	73.4	73.4	17.9	54.8					
4	S	86.09	72.33	73.81	72.20	76.69	17.10	13.90					
5	O	97.86	75.61	78.44	74.16	65.32	17.21	54.60	27.80	25.94	109.19		
5	S	81.16	76.66	78.53	75.15	66.05	17.32	13.24	28.12	26.28	109.55		
6	O	99.53	74.41	80.07	74.41	71.20	17.69	57.09	27.67	26.02	110.40		
6	S	81.80	76.09	79.95	74.28	74.91	17.41	14.26	27.58	25.98	109.92		
7	O	98.08	76.00	78.58	81.09	64.31	17.72	54.44	27.80	26.11	108.92	72.64	
7	S	81.68	76.85	78.48	81.39	65.31	17.89	13.17	27.99	26.35	109.21	72.97	
8	O	100.7	71.3	71.7	81.7	67.2	18.0	54.7				74.9	
8	S	85.28	71.86	72.39	81.77	67.72	17.87	13.36				74.68	
9	O	98.3	78.9	71.7	82.2	67.3	18.1	54.6				73.1	74.8
9	S	82.51	80.07	72.10	82.51	67.72	17.99	13.40				72.42	74.79
10	O	100.5	68.6	80.2	80.2	67.4	18.0	54.6				72.0	75.2
10	S	84.85	70.03	80.32	80.32	67.99	17.86	13.42				72.17	75.19
11	O	98.55	76.10	73.57	78.90	67.41	17.76	54.39				72.81	74.48
11	S	83.11	77.52	73.89	79.35	68.16	18.02	13.64				72.55	74.82

(continued)

^{13}C-NMR chemical shift data (ppm.) (Continued)

		C-1	C-2	C-3	C-4	C-5	C-6	XCH_3	C (ac)	CH_2Ph	Ref.
12	O	98.05	77.00	79.03	75.94	65.88	17.41	54.86	109.54		12
12	S	81.00	76.97	79.05	74.72	66.02	17.25	13.26	109.48		
13	S	81.89	77.12	80.24	74.58	75.16	17.61	14.61	110.13		
14	O	98.05	76.32	76.41	74.44	63.92	17.13				
14	S	81.07	76.96	76.15	74.67	64.83	17.18				
15	O	98.05	76.30	79.40	80.67	64.41	17.73	54.58	109.24	72.88	
15	S	81.29	77.19	79.26	81.29	65.36	17.83	13.23	109.35	73.18	
16	O	98.2	75.4	79.9	71.9	65.4	17.4	54.8	102.9		13
16	S	81.30	76.24	79.44	72.47	65.73	17.32	13.27	102.95		
17	O	98.1	78.5	78.1	74.6	65.9	17.4	54.7	104.1		13
17	S	81.03	78.99	78.11	75.47	66.13	17.28	13.25	104.04		
18	O	98.0	75.5	76.9	71.6	63.4	16.8	54.5	102.8		13
18	S	81.50	76.44	76.82	71.95	64.33	17.06	13.24	103.09		
19	O	97.8	77.9	75.0	75.4	63.6	16.8	54.4	104.3		13
19	S	81.03	78.79	75.39	75.48	64.39	17.11	13.30	104.59		
20	O	100.8	68.1	80.0	71.8	68.1	17.7	54.7		71.7	12
20	S	85.10	69.33	80.12	72.00	68.28	17.58	13.54		71.86	
21	O	98.6	78.5	71.7	73.7	68.2	17.7	54.6		73.1	12
21	S	82.54	79.67	72.12	74.32	68.31	17.57	13.56		72.38	

12-O afforded 15-O. All efforts to prepare methyl 2,3-O-diphenylmethylene-β-L-rhamnopyranoside failed, rather complete anomerization effected by pyridinium hydrochloride took place. The NMR data are summarized in the tables. The results of this comparison can be evaluated as follows: The O→S replacement at the anomeric carbon atoms causes a very strong upfield shift at C-1. Characteristic downfield shifts of ~1 ppm can be observed for C-2 atoms. The chemical shift values of the other skeleton carbon atoms are not sensitive to the O→S exchange at the anomeric centres.

A considerable difference was observed in $[\alpha]_D$-values of the O- and S-rhamnopyranoside derivatives. In the case of the α-anomers the thio-derivatives have substantially higher negative values, than do the oxygen-derivatives. On the other hand, the β-thio-rhamnopyranosides show higher positive values than the O-glycoside derivatives, but these differences are not so substantial.

The $[\alpha]_D$-values of the O- and S-rhamnopyranoside derivatives:

	1	2	3	4	5	6	7
O	-60	+45	-62	+95	-16	+78	-62
S	-101	+68	+114	-142	-142	+98	-147

	8	9	10	11	12	14	15
O	-68	-17	-46	+4.4	-72	-29	-83
S	-166	-82	-79	-46	-170	-118	-148

	16	17	18	19	20	21
O	-16	-23	-24	+30	-25	+3.6
S	-125	-128	-114	-71	-117	-67

EXPERIMENTAL

Melting points were determined on a Kofler apparatus and are uncorrected. Optical rotations were determined with a Perkin-Elmer 241

polarimeter. NMR spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si) with a Bruker WP-200 spectrometer at room temperature. TLC was performed on Kieselgel 60 F_{254} (Merck) with detection by charring with sulphuric acid. Short-column chromatography was effected on Kieselgel G (Reanal) adsorbent.

Methyl 2,3,4-Tri-O-acetyl-1-thio-α- (1-S) and -β-L-Rhamnopyranoside (2-S). A solution of 2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl bromide (10.0 g) in acetone (60 mL) was boiled under reflux with thiourea (7.0 g). After 1 h the solution was diluted with dichloromethane (150 mL) and stirred with an aqueous solution (150 mL) of a Na_2CO_3 (8.8 g) and Na_2SO_3 (5.5 g) for 1 h at 20 °C. The organic layer was separated and dried, and methyl iodide (6.75 mL) and N-ethyldiisopropylamine (9.3 mL) were added at room temperature. After 1 h the mixture was washed with water (3 x 50 mL), dried, and concentrated, to give a syrup. It was crystallized from ethanol (15 mL) to give 2-S (0.60 g, 6.6%): mp 189-190 °C, $[\alpha]_D$ +67° (c 0.70, chloroform), R_F 0.78 (dicloromethane-acetone, 97:3).

Anal. Calcd for $C_{13}H_{20}O_7S$: C, 48.74; H, 6.29; S, 10.00. Found: C, 48.88; H, 6.37; S, 9.86.

The residue was purified by column chromatography, to give 1-S (3.85 g, 46.3%):$[\alpha]_D$ -101° (c 1.0, chloroform), R_F 0.80.

Anal. Found: C, 48.71; H, 6.20; S, 10.12.

Methyl 1-Thio-α-L-rhamnopyranoside (3-S). Compound 1-S (2.3 g) in dry methanol (30 mL) was deacetylated in the prescence of NaOMe (5 mg). After 1 day the solution was neutralized with Amberlite IR-120 (H^+) resin, filtered, and concentrated to give 3-S. It was crystallized from ethyl acetate (1.25 g, 89.6%): mp 104-105 °C,$[\alpha]_D$ -185° (c 1.0, water), R_F 0.78 (dichloromethane-methanol, 8:2).

Anal. Calcd for $C_7H_{14}O_4S$: C, 43.28; H, 7.26; S, 16.50. Found: C, 43.11; H, 7.38; S, 16.45.

Methyl 1-Thio-β-L-rhamnopyranoside (4-S). Compound 2-S (0.25 g) in dry methanol (25 mL) was treated with NaOMe (5 mg) as described for 3-S, to give 4-S (0.13 g, 85.8%): mp 158 °C (from ethyl acetate),$[\alpha]_D$ +114°, (c 0.6, water), R_F 0.77 (dichloromethane-methanol, 8:2).

Anal. Calcd for $C_7H_{14}O_4S$: C, 43.28; H, 7.26; S, 16.50. Found: C, 43.27; H, 7.19; S, 16.39.

Methyl 2,3-O-Isopropylidene-1-thio-α-L-rhamnopyranoside (5-S). Methyl 1-thio-α-L-rhamnopyranoside (3-S, 4.15 g) was stirred in 2,2-dimethoxypropane (5 mL) in the presence of p-toluenesulphonic acid (30 mg) at 20 °C for 1 h. The mixture was then diluted with dichloromethane (50 mL), washed with 5% aqueous $NaHCO_3$ (20 mL) and water (3 x 10 mL), dried (Na_2SO_4) and concentrated, to give a crystalline product. It was recystallized from n-hexane-ether, to give 5-S (4.30 g, 85.0%): mp 76-77 °C, $[\alpha]_D$ -142° (c 0.8, chloroform), R_F 0.69 (dichloromethane-methanol, 95:5).

Anal. Calcd for $C_{10}H_{18}O_4S$: C, 51.26; H, 7,74; S, 13.68. Found: C, 51.10; H, 7.68; S, 13.39.

Methyl 2,3-O-Isopropylidene-1-thio-β-L-rhamnopyranoside (6-S). A solution of 4-S (0.79 g) in N,N-dimethylformamide (2 mL) was stirred with 2,2-dimethoxypropane (4.9 mL, 4.16 g) and p-toluenesulphonic acid (10 mg) for 16 h at room temperature. The work-up was as described for the preparation of 5-S to give 6-S (0.76 g, 79.7%): mp 73-74 °C (from light petroleum-ether, 3:1), $[\alpha]_D$ +99° (c 0.9, chloroform), R_F 0.55 (dichloromethane-methanol, 95:5).

Anal. Calcd for $C_{10}H_{18}O_4S$: C, 51.26; H, 7.74; S, 13.68. Found: C, 51,12; H, 7.80; S, 13.46.

Methyl 4-O-Benzyl-2,3-O-isopropylidene-1-thio-α-L-rhamnopyranoside (7-S). Compound 5-S (4.15 g) in N,N-dimethylformamide (30 mL) and in the presence of KOH (3.97 g) was treated with benzyl bromide (3.63 g, 2.52 mL) for 1 h at room temperature. The reaction mixture was diluted with dichloromethane (200 mL), filtered, and concentrated in vacuo. The residue was diluted with dichloromethane (200 mL), washed with water (3 x 20 mL), dried (Na_2SO_4), and concentrated, to give a crystalline product, which was recrystallized from ethanol, to give 7-S (4.29 g, 74.7%): mp 51-52 °C, $[\alpha]_D$ -147° (c 0.7, chloroform), R_F 0.50 (dichloromethane).

Anal. Calcd for $C_{17}H_{24}O_4S$: C, 62.93; H, 7.45; S, 9.88. Found: C, 62.96; H, 7.40; S, 9.71.

Methyl 4-O-Benzyl-1-thio-α-L-rhamnopyranoside (8-S). A solution of 7-S (2.8 g) in dichloromethane (50 mL) was hydrolyzed with trifluoroacetic acid (5 mL) in the presence of water (1 drop) for 1.5 h at 20 °C. It was diluted with dichloromethane (150 mL), washed with water until neutral (5 x 10 mL), dried, and concentrated. The residue was

crystallized from cyclohexane-light petroleum to give 8-S (2.36 g, 96.1%): mp 76 °C, $[\alpha]_D$ -166° (c 0.8, chloroform), R_F 0.65 (dichloromethane-methanol, 9:1).

Anal. Calcd for $C_{14}H_{20}O_4S$: C, 59.13; H, 7.08; S, 11.27. Found: C, 59.04; H, 7.21; S, 11.21.

Methyl 2,4-Di-O-benzyl-1-thio-α-L-rhamnopyranoside (9-S) and methyl 3,4-Di-O-benzyl-1-thio-α-L-rhamnopyranoside (10-S). A mixture of 8-S (4.2 g), tetrabutylammonium bromide (1.2 g), benzyl bromide (1.9 mL) in dichloromethane (150 mL) and aqueous sodium hydroxide (15 mL of 10% solution) was stirred with a high-speed magnetic stirrer at room temperature for 2 days. The organic layer was separeted, washed with water (3 x 20 mL), dried (Na_2SO_4) and concentrated. The residual syrup was chromatographed, to give, first, the syrupy 9-S (4.20 g, 75.9%): $[\alpha]_D$ -82° (c 0.7, chloroform), R_F 0.67 (dichloromethane-acetone, 95:5).

Anal. Calcd for $C_{21}H_{26}O_4S$: C, 67.35; H, 6.99; S, 8.56. Found: C, 67.22; H, 6.87; S, 8.39.

Continuing the elution, the syrupy 10-S was obtained as the second component (0.14 g, 2.5%):$[\alpha]_D$ -79° (c 2.2, chloroform), R_F 0.52

Anal. Found: C, 67.41; H, 7.08; S, 8.35.

Methyl 3-O-Acethyl-2,4-di-O-benzyl-1-thio-α-L-rhamnopyranoside (11-S). Compound 9-S (60 mg) was acetylated with pyridine (0.5 mL) and acetic anhidride (0.5 mL) at 20 °C for 24 h. Conventional work-up gave syrupy 11-S (65 mg, 97.4%): $[\alpha]_D$ -46° (c 1.1, chloroform), R_F 0.79 (dichloromethane-ethyl acetate, 95:5).

Anal. Calcd for $C_{23}H_{28}O_5S$: C, 66.32; H, 6.77; S, 7.69. Found: C, 66.41; H, 6.70; S, 7.52.

Methyl 2,3-O-Diphenylmethylene-1-thio-α-L-rhamnopyranoside (12-S). A solution of 3-S (0.87 g) in dry pyridine (15 mL) was stirred with dichlorodiphenylmethane (1.6 g, 1.3 mL) at 80 °C. After 24 h it was poured into ice-water (50 g) and the residue was dissolved in dichloromethane, washed with 0.5 M H_2SO_4 (3 x 30 mL) and water until neutral. The solution was dried (Na_2SO_4), filtered and concentrated to give a red-brown syrup. It was purified by column chromatography (dichloromethane-acetone, 98:2), to give 12-S wich was recrystallized from cyclohexane (0.80 g, 49.8%): mp 117 °C, $[\alpha]_D$ -170° (c 0.8, chloroform), R_F 0.55.

Anal. Calcd for $C_{20}H_{22}O_4S$: C, 67.01; H, 6.18; S, 8.94. Found: C, 67.18; H, 6.05; S, 8.76.

Methyl 2,3-O-Diphenylmethylene-1-thio-β-L-rhamnopyranoside (13-S). A solution of 4-S (0.38 g) in dry pyridine (10 mL) was stirred with dichlorodiphenylmethane (0.8 g, 0.65 mL) at 100 °C. After 48 h the work-up was as described for 12-S to give a syrup, which was purified by column chromatography, to give 13-S (125 mg, 18%): R_F 0.50 (dichloromethane-acetone, 95:5).

Anal. Calcd for $C_{20}H_{22}O_4S$: C, 67.01; H, 6.18; S, 8.94. Found: C, 66.88; H, 6.10; S, 8.79.

Methyl 4-O-Acetyl-2,3-O-diphenylmethylene-1-thio-α-L-rhamnopyranoside (14-S). Compound 12-S (0.7 g) was acetylated with pyridine (5 mL) and acetic anhydride (5 mL) at 20 °C for 16 h. Conventional work-up gave amorphous 14-S (0.75 g, 95.8%): $[\alpha]_D$ +118° (c 0.34, chloroform), R_F 0.80 (dichloromethane-ethyl acetate, 95:5).

Anal. Calcd for $C_{22}H_{24}O_5S$: C, 65.98; H, 6.04; S, 8.00. Found: C, 65.85; H, 6.12; S, 7.81.

Methyl 4-O-Benzyl-2,3-O-diphenylmethylene-1-thio-α-L-rhamnopyranoside (15-S). Compound 12-S (240 mg) in N,N-dimethylformamide (2 mL) and in the presence of KOH (120 mg) was treated with benzyl bromide (0.12 mL) at room temperature. After 1 h the work-up was done as described for 7-S to give a syrup, which was purified by column chromatography, to give 15-S (195 mg, 64.9%): $[\alpha]_D$ -148° (c 0.9 chloroform), R_F 0.57 dichloromethane-n-hexane, 7:3).

Anal. Calcd for $C_{27}H_{28}O_4S$: C, 72.29; H, 6.29; S, 7.14. Found: C, 72.11; H, 6.38; S, 7.19.

Methyl 4-O-Acetyl-endo- (19-S) and -exo-2,3-O-benzylidene-1-thio-α-L-rhamnopyranoside (18-S). Compound 3-S (1.1 g) was treated with α,α-dimethoxytoluene (8.6 mL) in the presence of p-toluenesulphonic acid (0.02 g) at room temperature for 1 h. Work-up, as described for 5-S, gave a syrup (1.2 g), which was fractionated by column chromatography, to give the mixture of 18-S and 19-S (0.86 g, 53.8%), R_F 0.65 (dichloromethane-acetone, 9:1). It was acetylated with pyridine (1.5 mL) and acetic anhydride (1.5 mL) at 20 °C for 24 h. Conventional work-up gave a crystalline product. Recrystallisation of the mixture from ethanol (4 mL) gave 18-S (0.27 g, 27.3%): mp 154 °C, $[\alpha]_D$ -114° (c 0.7, chloroform) R_F 0.40 (light petroleum-ethyl acetate, 4:1).

Anal. Calcd for $C_{16}H_{20}O_5S$: C, 59.24; H, 6.21; S, 9.88. Found: C, 59.35; H, 6.18; S, 9.74.

The residue in the mother liquid gave syrupy 19-S (0.31 g, 31.4%): $[\alpha]_D$ -71° (c 0.8, chloroform), R_F 0.47.

Anal. Found: C,59.40; H, 6.11; S, 9.79.

Methyl Exo-2,3-O-benzylidene-1-thio-α-L-rhamnopyranoside (16-S). A solution of 18-S (0.175 g) in dry methanol (10 mL) was deacetylated in the presence of NaOMe (5 mg). After 24 h, the solution was neutralized with Amberlite IR-120 (H^+) resin, filtered, and concentrated to give 16-S. It was recrystallized from ethanol (0.14 g, 92.5%): mp 122-124 °C, $[\alpha]_D$ -125° (c 0.6, chloroform), R_F 0.64 (dichloromethane-acetone, 9:1).

Anal. Calcd for $C_{14}H_{18}O_4S$: C, 59.55; H, 6.42; S, 11.35. Found: C, 59.49; H, 6.60; S, 11.21.

Methyl Endo-2,3-O-benzylidene-1-thio-α-L-rhamnopyranoside (17-S). A solution of 19-S (0.24 g) in dry methanol (10 mL) was treated with NaOMe (5 mg) for 24 h, then neutralized with Amberlite IR-120 (H^+) resin, filtered, and concentrated to give syrupy 17-S (0.20 g, 95.7%): $[\alpha]_D$ -1.5° (c 1.14, chloroform), R_F 0.64 (dichloromethane-acetone, 9:1).

Anal. Calcd for $C_{14}H_{18}O_4S$: C, 59.55; H, 6.42; S, 11.35. Found: C, 59.63; H, 6.48; S, 11.30.

Methyl 3-O-Benzyl-1-thio-α-L-rhamnopyranoside (20-S). Compound 16-S (85 mg) was hydrogenolyzed with $LiAlH_4$ (17 mg) and $AlCl_3$ (59 mg) in ether-dichloromethane (20 mL, 1:1) for 10 min at 20 °C. After the usual work-up the syrup was purified by column chromatography, to give 20-S (65 mg, 75.9%): $[\alpha]_D$ -117° (c 0.7, chloroform), R_F 0.53 (dichloromethane-acetone, 8:2).

Anal. Calcd for $C_{14}H_{20}O_4S$: C, 59.13; H, 7.08; S, 11.27. Found: C, 59.11; H, 7.00; S, 11.20.

Methyl 2-O-Benzyl-1-thio-α-L-rhamnopyranoside (21-S). Compound 17-S (0.14 g) was treated with $LiAlH_4$ (28 mg) and $AlCl_3$ (98 mg) in ether-dichloromethane (20 mL, 1:1) for 10 min at room temperature. After the usual work-up the product was purified by column chromatography, to give syrupy 21-S (73 mg, 51.7%): $[\alpha]_D$ -67° (c 0.9, chloroform), R_F 0.41 (dichloromethane-acetone, 8:2).

Anal. Calcd for $C_{14}H_{20}O_4S$: C, 59.13; H, 7.08; S, 11.27. Found: C, 59.03; H, 7.15; S, 11.11.

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