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Studies of Tritylated Pentoses and 6-Deoxyhexoses. II. Trityl Ethers of Methyl α- and β-L-Rhamnopyranoside and Their Derivatives[1]

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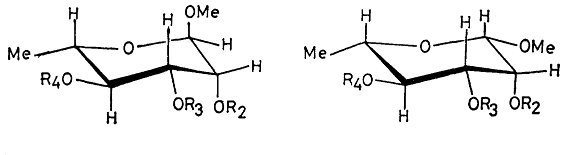
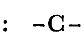
Synopsis. Mono-*O*-trityl derivatives of methyl α- and β-L-rhamnopyranoside have been prepared and the structures established by PMR analysis.

Hockett and Hudson[2] described the tritylation of methyl α-L-fucopyranoside which contains only secondary hydroxyl groups.

Recently, the preparation of methyl 2-*O*- and 3-*O*-trityl-α-D-fucopyranoside has been reported.[3] This paper represents on extention of that work and reports the tritylation of methyl α- and β-L-rhamnopyranoside.



1	$R_2=R_3=R_4=H$	**2**	$R_2=R_3=R_4=H$
3a	$R_3=Tr, R_2=R_4=H$	**11a**	$R_3=Tr, R_2=R_4=H$
3b	$R_3=Tr, R_2=R_4=Ac$	**11b**	$R_3=Tr, R_2=R_4=Ac$
3c	$R_3=Tr, R_2=R_4=Me$	**11c**	$R_3=Tr, R_2=R_4=Me$
4a	$R_4=Tr, R_2=R_3=H$	**12a**	$R_4=Tr, R_2=R_3=H$
4b	$R_4=Tr, R_2=R_3=Ac$	**12b**	$R_4=Tr, R_2=R_3=Ac$
4c	$R_4=Tr, R_2=R_3=Me$	**12c**	$R_4=Tr, R_2=R_3=Me$
5a	$R_2=Tr, R_3=R_4=H$	**13a**	$R_3=H, R_2=R_4=Me$
5b	$R_2=Tr, R_3=R_4=Ac$	**13b**	$R_3=Ac, R_2=R_4=Me$
6	$R_3=H, R_2=R_4=Ac$	**14a**	$R_4=H, R_2=R_3=Me$
7	$R_4=H, R_2=R_3=Ac$	**14b**	$R_4=Ac, R_2=R_3=Me$
8	$R_2=H, R_3=R_4=Ac$	Tr:	
9a	$R_3=H, R_2=R_4=Me$		
9b	$R_3=Ac, R_2=R_4=Me$		
10a	$R_4=Ac, R_2=R_3=Me$		
10b	$R_4=Ac, R_2=R_3=Me$		

Results and Discussion

The reaction of **1** with 2.5 molar equivalents of trityl chloride in pyridine afforded three mono-*O*-trityl ethers: the 3-*O*- (**3a**), 4-*O*- (**4a**) and 2-*O*-trityl derivative (**5a**) in 57, 2.8 and 1.4% yields, respectively, which were converted to the corresponding di-*O*-acetates **3b**, **4b**, and **5b**. The PMR spectra were analyzed with a favorable 1C conformation[4] confirming the structure. The PMR data for the compounds described are summarized in Tables 1 and 2. Detritylation of **3b**, **4b**, and **5b** with HBr in glacial acetic acid at low temperature gave the corresponding di-*O*-acetates: **6**, **7**, and **8**. Methylation of **3a** and **4a**, followed by detritylation and acetylation gave the *O*-acetyl-di-*O*-methyl derivatives **9b** and **10b**, the structures of which were established by PMR analysis. Gas chromatography-mass (GC-MS) spectra of the intermediary di-*O*-methyl derivatives (**9a** and **10a**) were similar to the

TABLE 2. CHEMICAL SHIFTS (ppm) OF METHYL PROTONS

	OAc (s, 3H)	OMe (s, 3H)	H-6 (d, 3H)
3b	1.85, 2.18	3.12	1.10
4b	1.18, 1.85	3.18	1.08
5b	1.88, 2.02	2.93	1.25
6	2.09, 2.13	3.33	1.19
7	2.04, 2.10	3.36	1.35
8	2.02, 2.06	3.37	1.20
3c		3.10, 3.14, 3.57	1.25
4c		2.85, 3.37, 3.43	1.05
9b	2.13	3.36, 3.45, 3.48	1.33
10b	2.08	3.40, 3.42, 3.52	1.20
11b	1.72, 1.92	3.32	1.19
12b	1.20, 1.92	3.34	1.16
11c		3.26, 3.26, 3.58	1.33
12c		2.84, 3.40, 3.43	1.09
13b	2.17	3.50, 3.52, 3.57	1.37
14b	2.07	3.42, 3.53, 3.62	1.25

TABLE 1. PMR PARAMETERS OF METHINE PROTONS

	Chemical shifts, δ/ppm					Coupling constants/Hz				
	H-1	H-2	H-3	H-4	H-5	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$
3b	4.43 (d)	4.18 (dd)	3.88 (dd)	5.27 (dd)	3.47 (qd)	1.9	3.2	10.0	9.7	6.0
4b	4.42 (d)[a)]	*ca.*5.2	*ca.*5.3	3.18 (dd)[b)]	4.03 (qd)	1.5	—	9.0	9.0	6.1
5b	3.53 (d)	3.88 (dd)	5.07 (dd)[c)]	5.44 (dd)	*ca.*3.7 (m)[d)]	1.6	3.0	10.5	9.0	6.0
6	4.63 (d)	5.02 (dd)	3.98 (dd)	4.82 (dd)	3.77 (qd)	1.5	4.0	9.8	10.0	6.0
7	4.58 (d)	4.9—5.3 (m)		3.4—3.9 (m)		1.8	—	—	—	6.0
8	4.66 (d)	4.01 (dd)	4.8—5.3 (m)		3.82 (qd)	1.6	3.0	—	9.5	6.0
9b	4.66 (d)	3.60 (dd)[f,g)]	5.08 (dd)	3.22 (dd)[g)]	3.67 (qd)	2.0	3.4	9.5	9.5	6.0
10b	4.75 (d)	3.3—3.6 (overlapped)		5.06 (dd)	3.85 (qd)	1.3	—	9.5	9.5	6.4
11b	3.89d (bs)	4.74 (d,bs)	3.48 (dd)	5.27 (dd)	*ca.*3.1 (m)	*ca.*0.5	3.4	10.0	10.0	6.2
12b	4.51 (d)	5.33 (dd)	5.01 (dd)	3.23 (dd)	3.70 (qd)	*ca.*0.7	3.3	9.5	9.5	6.0
13b	4.37 (d,bs)	3.1—4.1 (m)	4.77 (dd)	3.1—4.1 (m)		*ca.*0.5	3.0	10.0	—	6.0
14b	4.32 (d,bs)	3.1—3.9 (m)		5.02 (dd)	3.1—3.9 (m)	*ca.*0.5	—	10.0	10.0	6.2

Mutiplicity in nuclear magnetic double resonance (irradiated protons are in parentheses): a) s (H-2 and H-3); b) d (H-2and H-3); c) d (H-2); d) d (H-6); e) s (H-2); f) d (H-1); g) d (H-3); bs: broad singlet.

methyl 2,4- and 2,3-di-*O*-methyl-α-D-fucopyranosides,[3] respectively, supporting the proposed structures. The analogous triethylation of **2** gave a 2: 1 mixture of two mono-*O*-trityl ethers: 3-*O*- (**11a**) and 4-*O*- (**12a**), in a combined yield of 52%. The structures were established by PMR analysis of the corresponding di-*O*-acetates (**11b** and **12b**) and *O*-acetyl-di-*O*-methyl derivatives (**13b** and **14b**) of **2**. The equatorial OH-3 having a vicinal cis hydroxyl group (OH-2) was most reactive towards tritylation as shown in the selective acetylation of the pyranosides.[4]

Experimental

General Methods. The solution were evaporated under reduced pressure below 40 °C. Optical rotations were measured with a Japan Spectroscopic DIP-SL polarimeter. PMR spectra were recorded on a NEVA NV-14 (60 MHz) or Varian EM-360 (60 MHz) spectrometer, deuteriochloroform being used as the solvent and tetramethylsilane as an internal standard. The multiplicities of the signals have been designated s for a singlet, d for a doublet, dd for a doublet of doublets, qd for a quartet of doublets and m for a multiplet. GC-MS was conducted using the Varian MAT 111 GC/MS system. An electron energy of 80 eV was applied. A glass column (5′×1/8″) packed with 5% NPGS/Chromosorb W was used for the GC. TLC and preparative column chromatography were performed with Wakogel B-10 and C-300 (Wako Junyaku Co., Ltd.), respectively.

*Tritylation of Methyl α- (1) and β-*L*-Rhamnopyranoside (2).* Rhamnosides **1** and **2** were prepared from commercial L-rhamnose monohydrate. A mixture of **1** or **2** and trityl chloride in a molar ratio of 1: 2.5 dissolved in dry pyridine (×5) was allowed to stand for five days at room temperature. A small amount of water was added to the solution. After concentration, the residue was dissolved in (×5) toluene. Triphenylmethanol was filtered from the toluene solution and the triphenylmethanol-free concentrate subjected to recycling column chromatography five-times on silica gel (50 g) with 5% acetone/benzene. Evaporation of the solvent fractions having R_f values of 0.45, 0.42, and 0.39 on TLC in 15% acetone/benzene gave 973 mg (57.2%) of **3a**, 62 mg (3.7%) of **4a** and 29 mg (1.6%) of **5a**, respectively, as an amorphous solid. $[\alpha]^{20}_{\mathrm{D}}$ in chloroform: **3a**, −50.6° (*c* 2.7); **4a**, −88.4° (*c* 1.0); **5a**, +45.0° (*c* 1.1). Found: **3a**, C, 74.26; H, 6.82%; **4a**, C, 74.37; H, 6.79%; **5a**, C, 73.86; H, 6.73%. Calcd for $C_{26}H_{28}O_5$: C, 74.26; H, 6.71%.

The triphenylmethanol-free concentrate from **2** (1780 mg) was chromatographed on silica gel (50 g) with 5% acetone/benzene three-times. Concentration of the fractions having R_f values of 0.56 and 0.37 on TLC with 12.5% acetone/benzene two developments gave 1522 mg (36.5%) of **11a** and 633 mg (16.7%) of **12a** as an amorphous solid, respectively. $[\alpha]^{20}_{\mathrm{D}}$ in chloroform: **11a**, +55.2° (*c* 0.9); **12a**, +13.2° (*c* 0.7). Found: **11a**, C, 74.26; H, 6.71%; **12a**, C, 73.94; H, 6.80%. Calcd for $C_{26}H_{28}O_5$: C, 74.26; H, 6.71%. Compound **12a** was recrystallized as a monobenzene complex from benzene: $[\alpha]^{20}_{\mathrm{D}}$ +14.7° (*c* 1.2, chloroform), mp 67—68 °C. Found as a benzene complex: C, 77.65; H, 7.07%. Calcd for $C_{32}H_{34}O_5$: C, 77.52; H, 6.87%.

Acetylation of Methyl O-*Tritylrhamnopyranoside.* Each sample was acetylated under standard conditions for 2 days. After chromatographic purification, the acetates were recrystallized (except **4b** and **5b**) from 80% aqueous acetone in yields of 70—80%. Mp: **3b**, 127—130 °C; **11b**, 188—190 °C; **12b**, 186—188 °C. $[\alpha]^{20}_{\mathrm{D}}$ in chloroform: **3b**, −7.9° (*c* 3.3); **4b**, −86.7° (*c* 0.7); **5b**, +31.6° (*c* 0.5); **11b**, +53.6° (*c* 1.1); **12b**, −42.3° (*c* 1.35). Found: **3b**, C, 71.12; H, 6.61%; **4b**, C, 71.16; H, 6.44%; **5b**, C, 71.11; H, 6.51%; **11b**, C. 71.16; H, 6.46%; **12b**, C, 71.15; H, 6.46%. Calcd for $C_{30}H_{32}O_7$: C, 71.41; H, 6.40%.

Detritylation of Tritylacetyl Derivatives of Methyl Rhamnopyranosides. The detritylation procedure for **3b**, **4b**, and **5b** was almost identical to that for the tritylacetylsucroses.[6] The corresponding di-*O*-acetates were purified on a silica-gel column eluted with 5% acetone/benzene. The yields of detritylation products were 80—85%. Recrystallization (except 7) from 80% aqueous acetone gave the products as needles. Mp: **6**, 116 °C; **8**, 119—120 °C. $[\alpha]^{20}_{\mathrm{D}}$ in chloroform: **6**, −106.5° (*c* 1.7); **8**, −97.4° (*c* 1.0). Found: **6**, C, 75.24; H, 7.12%; **8**, C, 74.91; H, 7.17%. Calcd for $C_{28}H_{32}O_5$: C, 74 97; H, 7.19%.

Methylation of Methyl O-*Tritylrhamnopyranosides.* Methylation was conducted according to the Purdie method.[7] The products were purified on a silica-gel column eluted with 1% acetone/benzene, after the column was washed with benzene. The yields were approximately 70%. Recrystallization from 80% aqueous acetone gave the products as needles Mp: **3c**, 101—104 °C; **4c**, 138—139 °C; **11c**, 158—159 °C; **12c** 174—178 °C. $[\alpha]^{20}_{\mathrm{D}}$ in chloroform: **3c**, −30.0° (*c* 6.7); **4c**, −96.5° (*c* 0.7); **11c**, +67.3° (*c* 2.7); **12c**, +18.5° (*c* 1.5). Found: **3c**, C, 75.24; H, 7.12%; **4c**, C, 74.81; H, 7.17%; **11c**, C, 74.72; H, 7.17%; **12c**, C, 74.81; H, 7.19%. Calcd for $C_{28}H_{32}O_5$: C, 74.97; H, 7.19%.

Detritylation of Methyl O-*Trityl-di*-O-*methylrhamnopyranoside and Acetylation of the Corresponding Methyl Ethers.* Detritylation was conducted by heating the sample with 80% aqueous acetic acid at 90 °C for 1 h. The corresponding methyl ethers were purified on a silica-gel column eluted with 20% acetone/benzene. After acetylation of the methyl ethers, the corresponding acetates were purified on a silica-gel column, the acetates being eluted with 3% acetone/benzene after the column was washed with benzene. The yields of detritylation and acetylation products were greater than 90%. Mp: **13a**, 73.5 °C; **14a**, 63—64 °C; **14b**, 83—84 °C. $[\alpha]^{20}_{\mathrm{D}}$: **9a**, −63.2° (*c* 1.2, methanol); −53.3° (*c* 1.2, chloroform); lit,[8] $[\alpha]^{22}_{\mathrm{D}}$ −68.0° (*c* 4.1, methanol); **9b**, −46.5° (*c* 0.8, chloroform); lit,[3] −51.1° (*c* 0.8, chloroform); **10a**, −22.8° (*c* 1.0, methanol); −18.2° (*c* 1.0, chloroform); lit,[9] $[\alpha]_{\mathrm{D}}$ −14° (*c* 1.94, methanol); **10b**, −32.5° (*c* 1.4, chloroform); **13a**, +88.2° (*c* 1.4, chloroform); **13b**, +89.9° (*c* 1.4, chloroform); **14a**, +68.3° (*c* 3.2, chloroform); **14b**, +89.2° (*c* 2.3, chloroform). Found: **10b**, C, 53.40; H, 7.60%, **13b**, C, 53.17; H, 7.92%, **14b**, C, 53.72; H, 7.49%. Calcd for $C_{11}H_{20}O_6$: C, 53.21; H, 8.12%.

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