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A Facile Synthesis of 5-Thio-L-fucose and 3-O-Allyl-L-fucose Triacetate from D-Arabinose

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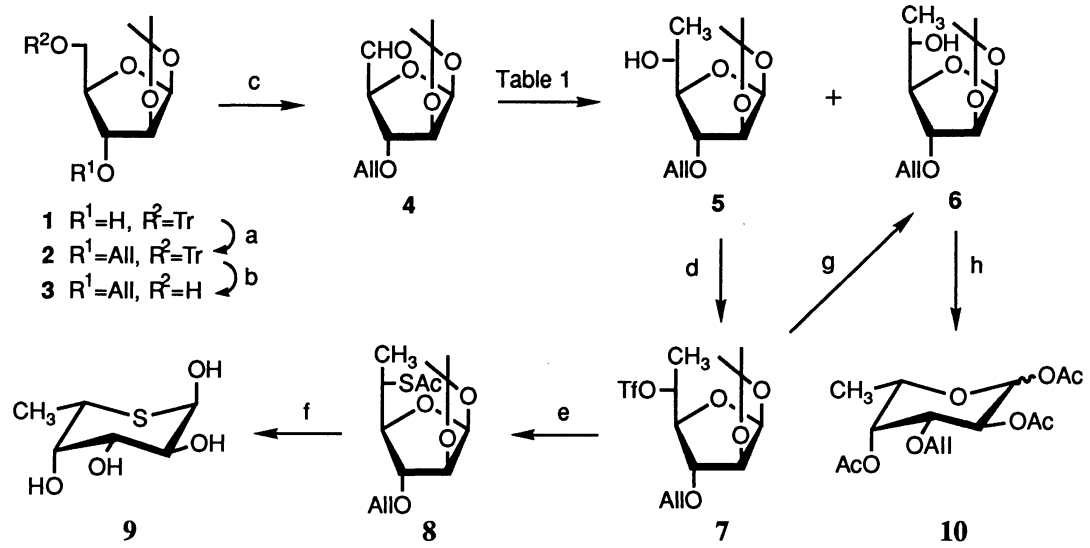
5-Thio-L-fucose and 3-*O*-allyl-L-fucose triacetate were synthesized from D-arabinose *via* D-*arabino*-pentodialdo-1,4-furanose derivative.

5-Thio-L-fucose (**9**) is one of ring oxygen substituted analogs and was found to have the most remarkable inhibitory activity[1] against glycosidase among the known 5-thiosugars. This indicates a potential usefulness of 5-thio-L-fucose derivatives for study of molecular recognition of oligosaccharide chain having L-fucopyranosyl residue. However, our first[1] and recent[2] syntheses of **9** from D-glucose require many steps. In this paper we would like to report a facile synthesis of **9** and also an alternative[3] synthetic intermediate (**10**) of 3-*O*-glycosylated L-fucopyranosyl residue as involved in the lipooligosaccharides[4] from *Mycobacterium kansasii*.

3-*O*-Allyl-1,2-*O*-isopropylidene-β-D-*arabino*-pentodialdo-1,4-furanose (**4**),[5] a key intermediate for one-carbon elongation at C-5, was derived from D-arabinose in 5 steps by following reaction sequences. Treatment of D-arabinose with trityl chloride in pyridine followed by isopropylidenation with 2,2-dimethoxypropane and *p*-toluenesulfonic acid in chloroform gave a furanose derivative **1** in 55% yield in 2 steps. The furanose **1** was converted successively to the 3-allyl ether **2** (76%), to the de-*O*-tritylated derivative **3** (87%), and then by Swern oxidation to the dialdose **4** (90%) as shown in Scheme 1.

Addition reactions of **4** with some methyl metal reagents, *i.e.*, MeMgI, MeLi, and Me_3Al, were examined and the results are summarized in Table 1. In all cases, the 5-(*R*)-isomer, *i.e.*, D-*altro* isomer **5** predominated over the 5-(*S*)-isomer, *i.e.*, L-*galacto* isomer **6**. Except one case (entry 2) the lower temperature favors the formation of **5** (entries 4 and 6). The best selectivity



a: AllBr, NaH/DMF, b: $Me_2C(OMe)_2$, TsOH · $H_2O/CHCl_3$, c: DMSO, $(COCl)_2/CH_2Cl_2$, d: Tf_2O, pyridine/CH_2Cl_2, e: AcSK/DMF, f: 1) MeONa/MeOH, 2) 70% AcOH, 3) Pd-C/H_2O, TsOH, g: 1) AcONa/DMF, 2) MeONa/MeOH, h: 1) 70% AcOH, 2) Ac_2O/pyridine

Scheme 1.

was observed with MeLi in ether at -78 °C and with Me_3Al (entries 6 and 7). In the cases[6] of MeMgI and MeLi, the stereoselectivity can be explained by the favored chelation of methyl metal reagents between the carbonyl oxygen and the oxygen at C-3 (6-membered ring)[7] as shown in the Fig. 1 rather than the ring oxygen (5-membered ring).[8] The 6-membered chelation is deduced to be preferred because the 5-membered chelation is sterically hindered due to the presence of 1,3-dioxolane rings attached to the same face of the furanose ring. The

Table 1. Stereoselectivity in the addition reactions of **4** with some methyl metal reagents

Entry	Me-M	Solvent	Temp °C	Time min	Yield %	5/6 [a]
1	MeMgI	Et_2O	0	30	82	3:2
2	MeMgI	Et_2O	-78	60	89	3:2
3	MeMgI	THF	0	10	54	4:1
4	MeMgI	THF	-20	120	70	8:1
5	MeLi	Et_2O	0	180	70	6:1
6	MeLi	Et_2O	-78	30	77	>10:1
7	Me_3Al	CH_2Cl_2-hexane	-70 - -10	240	63	>10:1

a) The ratio was determined by the intensities of two isomeric 6-methyl signals in ^{1}H-NMR.

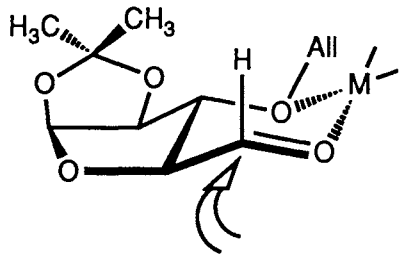


Fig. 1. Possible chelation of MeMgI and MeLi to the dialdose **4**.

mixture of **5** and **6** could be separated as the 5-acetates,[9] but the furtherconversion could be carried out using the mixture of addition products obtained under the conditions of entry 6. The introduction of sulfur atom at C-5 was done by substitution of 5-triflate **7** with potassium thiolacetate to give **8** in 48% yield (from the product mixture of entry 6) and conventional deprotection of **8**, that is, de-*S*-acetylation, acid hydrolysis of the acetal, and de-*O*-allylation gave known **9**[1] in good yields.

On the other hand, L-*galacto* isomer **6** is useful as an intermediate for such potential 3-*O*-protected glycosyl donor as per-*O*-acetylated 3-*O*-allyl-L-fucopyranose **10**. The isomer **5** could be also converted to **6** *via* **7** in 63% yield. Further, the donor **10** was prepared in 64% yield by hydrolysis of **6** followed by acetylation.

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References

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4) S. W. Hunter, I. Jardine, D. L. Yanagihara, and P. J. Brennan, *Biochemistry*, **24**, 2798 (1985).
5) All new compounds gave satisfactory elemental analysis and spectroscopic data. Data for some key compounds: **2**, $[\alpha]_D^{21}$ -6.7°C (*c*1.0, $CHCl_3$); ^1H NMR $\delta(CDCl_3)$.

7.57-7.22(m, Tr), 5.86(d, *J*4.0Hz, H-1), 6.12-5.60, 5.43-5.16 and 4.34-4.00(each m, All, H-3 and H-4), 4.55(d, H-2), 3.46-3.12(m, H-5, 5'), 1.25 and 1.19(each s, Isp), **4**, ^{1}H NMR δ($CDCl_3$), 9.77(s, H-5), 6.05(d, *J*3.5Hz, H-1); **5**, $[\alpha]_D^{21}$ +8.9 ℃ (*c*1.0, $CHCl_3$), ^{1}H NMR δ(acetone-d_6), 6.11-5.72, 5.41-5.05, and 4.16-3.61 (each m, All, H-3, H-4 and H-5), 5.84(d, *J*4.0Hz, H-1), 4.61 (d, H-2), 1.43 and 1.27 (each s, Isp), 1.19(d, *J*5.9Hz, H-6); **6**, ^{1}H NMR δ(acetone-d_6), 5.84(d, *J*4.2Hz, H-1), 4.65(d, H-2), 1.47 and 1.30(each s, Isp), 1.15(d, *J*6.2Hz, H-6); **8**, δ($CDCl_3$), 5.76(d, *J*3.7Hz, H-1), 2.34(s, SAc)1.40(d, *J*6.8Hz, H-6); **10**($CDCl_3$), δ6.31(d, *J*3.5Hz, H-1α), 5.64(d, *J*8.4Hz, H-1β), 1.23(d, *J*6.2Hz, H-6β), 1.16(d, *J*6.3Hz, H-6α).

6) In the case of Me_3Al a similar conformer but non-chelated one seems to be reasonable.

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9) The epimeric mixture of 5-acetates was separated on silica-gel column with CH_2Cl_2-toluene (3:1). Deacetylation of each component gave **5** and **6** in pure state.

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