

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

Hironobu HASHIMOTO* and Masayuki IZUMI

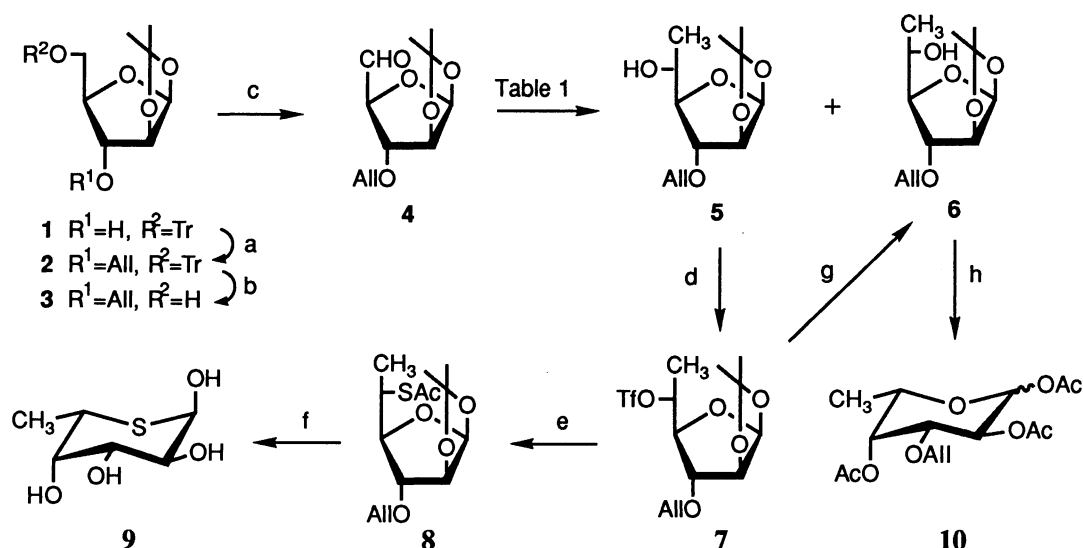
Department of Life Science, Faculty of Bioscience and Biotechnology,
Tokyo Institute of Technology, Nagatsuta, Midori-ku, Yokohama 227

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 activity¹⁾ 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 first¹⁾ and recent²⁾ 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 alternative³⁾ synthetic intermediate (**10**) of 3-*O*-glycosylated L-fucopyranosyl residue as involved in the lipooligosaccharides⁴⁾ 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 Me₃Al, 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: AlI_3 , NaH/DMF , b: $Me_2C(OMe)_2$, $TsOH \cdot H_2O/CHCl_3$, 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 $-78^\circ C$ and with Me_3Al (entries 6 and 7). In the cases⁶⁾ 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 1H -NMR.

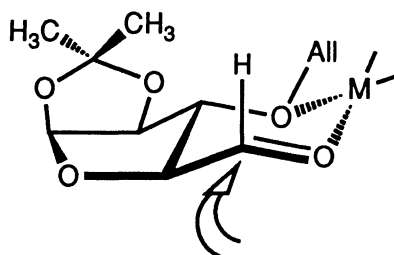


Fig. 1. Possible chelation of MeMgI and MeLi to the dialdose **4**.

mixture of **5** and **6** could be separated as the 5-acetates,⁹⁾ but the further conversion 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.

This work was supported in part by a Grant-in-Aid for Scientific Research on Priority Areas (No. 02250216) from the Ministry of Education, Science and Culture.

References

- 1) H. Hashimoto, T. Fujimori, and H. Yuasa, *J. Carbohydr. Chem.*, **9**, 683 (1990).
- 2) Via D-altrose monothioacetal derivative: cf. H. Hashimoto, M. Kawanishi, and H. Yuasa, *Tetrahedron Lett.* (in press).
- 3) A. Aqeel, K. Sato, H. Hashimoto, and J. Yoshimura, *J. Carbohydr. Chem.*, **8**, 405 (1989).
- 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**, $[\alpha]_{\text{D}}^{21} -6.7^{\circ}\text{C}$ (c 1.0, CHCl_3); ^1H NMR $\delta(\text{CDCl}_3)$.

7.57-7.22(m, Tr), 5.86(d, $J_{4.0\text{Hz}}$, 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**, $^1\text{H NMR}$ $\delta(\text{CDCl}_3)$, 9.77(s, H-5), 6.05(d, $J_{3.5\text{Hz}}$, H-1); **5**, $[\alpha]_{\text{D}}^{21} +8.9^\circ\text{C}$ ($c_{1.0}$, CHCl_3), $^1\text{H NMR}$ $\delta(\text{acetone-}d_6)$, 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, $J_{4.0\text{Hz}}$, H-1), 4.61 (d, H-2), 1.43 and 1.27 (each s, Isp), 1.19(d, $J_{5.9\text{Hz}}$, H-6); **6**, $^1\text{H NMR}$ $\delta(\text{acetone-}d_6)$, 5.84(d, $J_{4.2\text{Hz}}$, H-1), 4.65(d, H-2), 1.47 and 1.30(each s, Isp), 1.15(d, $J_{6.2\text{Hz}}$, H-6); **8**, $\delta(\text{CDCl}_3)$, 5.76(d, $J_{3.7\text{Hz}}$, H-1), 2.34(s, SAc)1.40(d, $J_{6.8\text{Hz}}$, H-6); **10**(CDCl_3), δ 6.31(d, $J_{3.5\text{Hz}}$, H-1 α), 5.64(d, $J_{8.4\text{Hz}}$, H-1 β), 1.23(d, $J_{6.2\text{Hz}}$, H-6 β), 1.16(d, $J_{6.3\text{Hz}}$, H-6 α).

- 6) In the case of Me_3Al a similar conformer but non-chelated one seems to be reasonable.
- 7) H. C. Jarell and W A. Szarek, *Carbohydr. Res.*, **67**, 43 (1978).
- 8) M. L. Wolfrom and S. Hanessian, *J. Org. Chem.*, **27**, 1800 (1962).
- 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.

(Received October 1, 1991)