Carbohydrate Research, 90 (1981) C1–C3
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

Preliminary communication

A rapid synthesis of *p*-nitrophenyl 2-*O*-α-L-fucopyranosyl-β-D-galactopyranoside*

KHUSHI L. MATTA, CONRAD F. PISKORZ and JOSEPH J. BARLOW
Department of Gynecology, Roswell Park Memorial Institute, Buffalo, NY 14263 (U.S.A.)

(Received December 30th, 1980; accepted for publication, January 16th, 1981)

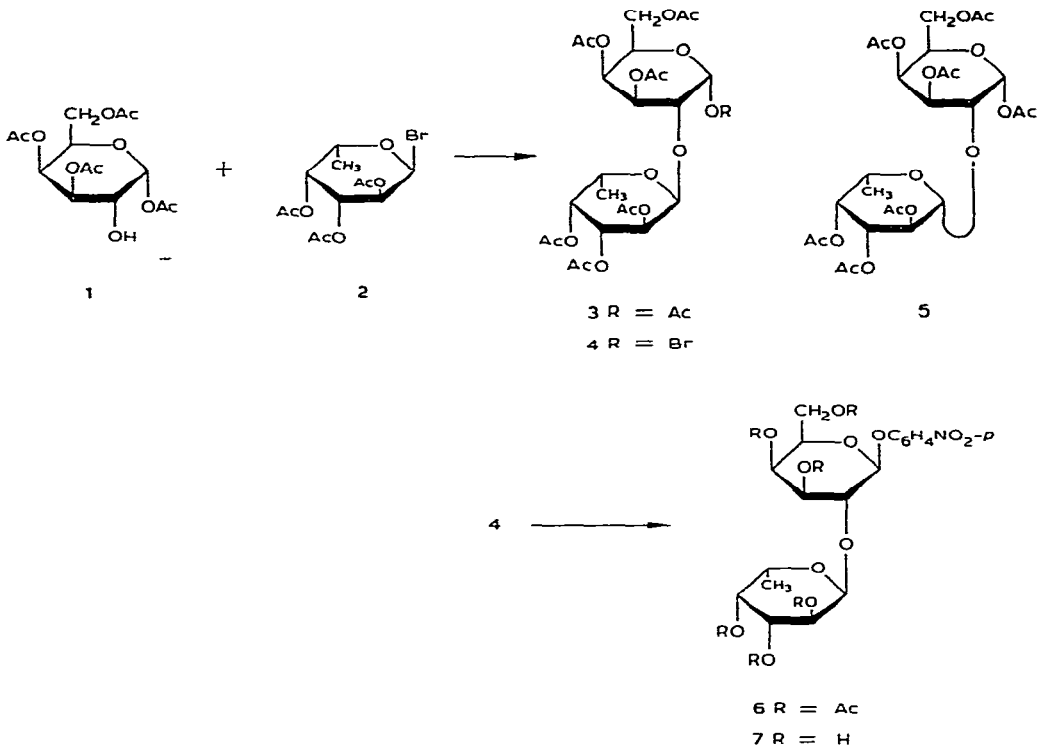
Recently, we reported[2] the use of synthetic *p*-nitrophenyl 2-*O*-α-L-fucopyranosyl-β-D-galactopyranoside as a substrate for the rapid detection of α-L-fucosidase having a stringent substrate-specificity for the α-(1→2)-linkage. According to Chester et al.[3], an α-(1→2)-fucosyltransferase present in human serum acts on aryl β-D-galactosides to give the corresponding aryl 2-*O*-α-L-fucopyranosyl-β-D-galactopyranosides. Indeed, the availability of the title disaccharide and of *o*-nitrophenyl 2-*O*-α-L-fucopyranosyl-β-D-galactopyranoside as reference compounds has led to the development of a facile, assay procedure for this unique, human (1→2)-α-L-fucosyltransferase[4]. We now describe a rapid synthesis of the title compound.

In our previous approach[1] for the synthesis of the desired compound, *p*-nitrophenyl 3,4,6-tri-*O*-acetyl-β-D-galactopyranoside in anhydrous acetonitrile was treated with 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide (2) in the presence of mercuric cyanide, to give a mixture of *p*-nitrophenyl 3,4,6-tri-*O*-acetyl-2-*O*-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-β-D-galactopyranoside and *p*-nitrophenyl 3,4,6-tri-*O*-acetyl-2-*O*-(2,3,4-tri-*O*-acetyl-β-L-fucopyranosyl)-β-D-galactopyranoside[2]. The anomeric mixture was separated by preparative, silica-gel chromatography. Reaction of *p*-nitrophenyl 6-*O*-benzoyl-3,4-*O*-isopropylidene-β-D-galactopyranoside with 2 under similar conditions, also gave a mixture of the corresponding α,β-disaccharide derivatives, and preparative, silica-gel chromatography had to be applied for their separation[5]. However, we had reported earlier[6] that reaction of the readily accessible 1,3,4,6-tetra-*O*-acetyl-α-D-galactose (1) and glycosyl halide 2 gave a mixture of anomers (3 and 5) which could be effectively separated by fractional recrystallization, and additional amounts of the α anomer 3 could be obtained by silica chromatography of the remaining mother liquor on a column of silica gel. Thus, for the large-scale preparation of the disaccharide, acetate 3 was considered to be a suitable starting-material.

Recently, use of bromotrimethylsilane for the preparation of a glycosyl bromide has been recommended[7]. In our hands, treatment of 3 with an excess of this reagent in benzene gave a mixture of 3,4,6-tri-*O*-acetyl-2-*O*-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-α-D-galactopyranosyl bromide (4) and starting material 3. However, treatment of com-

*Synthetic Studies in Carbohydrates. Part XVII. For Part XVI, see ref. 1.

0008-6215/81/0000–0000/$ 02.50,



pound 3 in anhydrous dichloromethane with hydrogen bromide in acetic acid gave the desired bromide 4 as the main product.

Thus, in a typical experiment, a solution of 3 (0.2 g) in anhydrous dichloromethane (10 ml) was treated with hydrogen bromide in acetic acid (4 ml) and the mixture was kept for 4 h at 0°, diluted with dichloromethane (50 ml), successively washed with a cold, saturated solution of sodium hydrogencarbonate and cold water (until neutral), dried (sodium sulfate), suspension filtered, and the filtrate evaporated, to give 0.2 g of 4 as a syrup. T.l.c. in 3:1 benzene–acetone showed a major spot, free from starting material but contaminated with some minor impurities.

A solution of bromide 4 (0.2 g) in 2-propanol (4 ml) and dichloromethane (1 ml) was stirred overnight with Amberlyst A-26 *p*-nitrophenoxide[8] (0.5 g), the suspension diluted with dichloromethane (10 ml), and filtered, and the filtrate evaporated, to give a syrup which, on treatment with ether–pentane, afforded 6 as amorphous material (0.2 g), $[\alpha]_D$ −108° (*c* 1, $CHCl_3$); lit.[1] $[\alpha]_D$ −113°. The i.r.- and n.m.r.-spectra were identical with those of our previous samples, prepared by the aforementioned methods. Deacylation of 6 in methanol in the presence of triethylamine, in the usual way, gave crystalline *p*-nitrophenyl 2-*O*-α-L-fucopyranosyl-β-D-galactopyranoside (7), identical with a previous sample. Thus, the present method provides an efficient synthesis of the title compound. Moreover, preparation of bromide 4 affords an intermediate of great potential importance.

REFERENCES

1 S. S. Rana, J. J. Barlow, and K. L. Matta, *Carbohydr. Res.*, 91 (1981) 149–157.
2 R. R. DiCioccio, C. F. Piskorz, G. Salamida, J. J. Barlow, and K. L. Matta, *Anal. Biochem.*, in press.
3 M. A. Chester, A. D. Yates, and W. M. Watkins, *Eur. J. Biochem.*, 69 (1976) 583–592.
4 R. A. DiCioccio, J. J. Barlow, and K. L. Matta, *Clin. Chim. Acta*, 108 (1980) 41–48.
5 K. L. Matta, unpublished results.
6 K. L. Matta, *Carbohydr. Res.*, 31 (1973) 410–412.
7 J. Thiem and B. Meyer, *Chem. Ber.*, 113 (1980) 3075–3085.
8 T. Iversen and R. Johansson, *Synthesis*, (1979) 823–824.