Carbohydrate Research, 167 (1987) c8–c10
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

Preliminary communication

The effect of high pressure on glycosylation under Helferich conditions

NIKOLAY K. KOCHETKOV, VICTOR M. ZHULIN, NELLY M. MALYSHEVA, EVGENY M. KLIMOV, AND ZINAIDA G. MAKAROVA

N. D. Zelinsky Institute of Organic Chemistry, Academy of Sciences of the U.S.S.R., Moscow (U.S.S.R.)

(Received May 8th, 1987; accepted for publication, June 25th, 1987)

The application of high pressure markedly affects the glycosylation of trityl ethers with 1,2-*O*-cyanoethylidene derivatives of sugars and resulted in the exclusive formation of 1,2-*trans*-glycosidic linkages even when the reaction at atmospheric pressure was non-specific[1,2]. The use of high pressure in the synthesis of polysaccharides *via* the trityl–cyanoethylidene polycondensation method has yielded[2] stereoregular homopolysaccharides with a higher d.p. The application of high pressure also affects the stereochemistry of other glycosylation reactions and we now report preliminary data on glycosylation under Helferich conditions as exemplified by the synthesis of glucopyranosyl-glucoses containing (1→6), (1→4), (1→3), and (1→2) linkages.

The reactions of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**1**) with methyl D-glucopyranoside triacetates variously having the free hydroxyl group at positions 2, 3, 4, and 6 were carried out under standard conditions, *i.e.*, using equimolar amounts of the reagents and $Hg(CN)_2$ in acetonitrile at 20°, both at normal and high pressure. Each high-pressure reaction was performed in a Teflon ampoule which was hermetically sealed, cooled in liquid nitrogen (to prevent reaction prior to the application of pressure), and placed in a high-pressure reactor[3]. Conventional work-up gave a mixture of disaccharides which was isolated by column chromatography on SiO_2. The ratio of 1,2-*trans*- and 1,2-*cis*-linked disaccharides was determined on the basis of the integrated intensity of the signals for C-1 of the non-reducing unit in the ^{13}C-n.m.r. spectra (Bruker WM-250 spectrometer). The results are given in Table I.

These data demonstrate a marked effect of high pressure on the result of the glycosylation, *i.e.*, the reaction is shifted extensively towards the formation of the 1,2-*trans*-glycosidic linkage. The ratio of 1,2-*trans*- and 1,2-*cis*-glycosides increased in all the reactions and the results obtained at pressures of 8 and 12 kbar were almost identical. The total yield of disaccharides in the reaction carried out under high pressure varied to some extent an this effect merits further investigation.

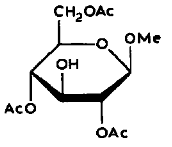
0008-6215/87/$ 03.50

TABLE I

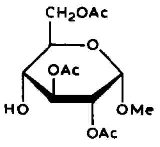
SYNTHESIS OF DISACCHARIDES BY HELFERICH GLYCOSYLATION[a]

Glycosyl donor	*Glycosyl acceptor*	*Pressure (kbar)*	*Reaction time (h)*	*Yield of disaccharides (%)*	*Ratio*
1	**3**	0.001	42	26	52:48
		8	20	45	79:21
		12	20	50	80:20
1	**4**	0.001	50	38	20:80
		12	24	32	80:20
1	**5**	0.001	45	74	72:28
		8	45	50	91:11
		12	45	47	94:6
1	**6**	0.001	28	73	*trans* only
		12	20	73	*trans* only
2	**7**	0.001	20	44	12:88
		8	20	32	38:62

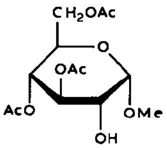
[a] Acylglycosyl halide (0.2 mmol), glycosyl acceptor (0.2 mmol), and $Hg(CN)_2$ (0.2 mmol) in MeCN (3.8 mL) at 20°.



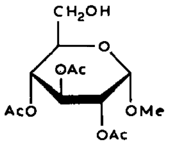
3



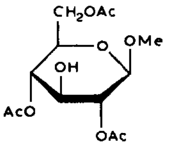
4



5



6



7

The reasons for the shift of glycosylation under high pressure towards the formation of the 1,2-*trans*-glycosidic linkage are unclear. Increase in pressure appears to shift the equilibrium between the acyloxonium ion and the glycosyl cation towards the former, thus favouring the formation of the 1,2-*trans*-glycosidic linkage. The same explanation has been proposed for a similar effect on the trityl–cyanoethylidene condensation. This explanation is supported by the value of the volume effect (-11 cm^3/mol) for the isomerisation of glycosyl cation into acyloxonium ion, which shows that the conversion of a monocyclic glycosyl cation into the bicyclic acyloxonium ion results in a decrease of the volume by this amount[4]. However, glycosylation was shifted towards the formation of 1,2-*trans*-glycoside even when an acyloxonium ion could not be formed. Thus, increase of pressure increases the 1,2-*trans*/1,2-*cis* ratio in the reaction of 3,4,6-tri-*O*-acetyl-2-*O*-methyl-α-D-glucopyranosyl bromide (**2**) with methyl 2,4,6-tri-*O*-acetyl-β-D-glucopyranoside.

The application of high pressure to the Helferich reaction, the stereochemical outcome of which is often unpredictable, results in the preferential formation of the 1,2-*trans*-glycosidic linkage, which has value in synthesis.

REFERENCES

1 V. M. Zhulin, E. M. Klimov, Z. G. Makarova, N. N. Malysheva, and N. K. Kochetkov, *Dokl. Akad. Nauk SSSR*, 289 (1986) 105–108.

2 N. K. Kochetkov, V. M. Zhulin, E. M. Klimov, N. N. Malysheva, Z. G. Makarova, and A. Ya. Ott, *Carbohydr. Res.*, 164 (1987) 241–254.

3 V. M. Zhulin, A. P. Suprun, G. P. Lopatina, T. A. Soboleva, A. S. Shashkov, M. G. Gonikberg, and G. P. Shakhovskoi, *Vysokomol. Soedin., Ser. A*, 13 (1971) 2518–2525.

4 V. M. Zhulin, Z. G. Makarova, E. M. Klimov, N. N. Malysheva, and N. K. Kochetkov, *Dokl. Akad. Nauk SSSR*, 296 (1987) 21