© Elsevier Scientific Publishing Company, Amsterdam - Printed in Belgium

Preliminary communication

Monobenzylation of diols using phase-transfer catalysis

PER J. GAREGG, TOMMY IVERSEN, and STEFAN OSCARSON

Department of Organic Chemistry, Arrhenius Laboratory, University of Stockholm, S-104 05 Stockholm (Sweden)

(Received June 16th, 1976; accepted for publication, July 5th, 1976)

Partial benzylation of monosaccharide diols is frequently used in order to obtain derivatives containing only one free hydroxyl group. The latter are useful intermediates for a variety of purposes such as the synthesis of disaccharides, aldehydo and keto sugars, and amino sugars, and for the inversion of configuration of the remaining hydroxyl group.

In order to obtain monobenzylated products from diols, for example a methyl 4,6-O-benzylidenehexoside, several strategies may be employed. These include the use of a limited reaction time, or a limited amount of alkylating agent or base. One useful system is partial benzylation with a limited amount of benzyl bromide in N,N-dimethyl-formamide using silver oxide as base. The product distribution depends on the relative reaction rate constants of the hydroxyl groups in the diol as well as on the relative reaction rate constants of the monoalkylated products. Statistical equations describing the product composition in homogeneous solution, expressed in terms of all the relative rate constants involved, have been developed by Spurlin¹. The equations can be simplified for diols², and show that the yields of monoalkylated products.

We now report three examples showing that the total yield of monobenzylated product may be raised substantially by using phase-transfer catalysis³. For the present case, the fundamental equilibrium is

 $Q_{aq}^{+} + RO_{aq}^{-} \Rightarrow QOR_{org}$,

where Q_{aq}^+ and RO_{aq}^- are the molar concentrations of tetra-alkylammonium cation and alcoholate anion, respectively, in the aqueous phase, and QOR_{org} is the molar concentration of the corresponding ion-pairs in the organic layer. Provided that a correct choice of solvents is made, the monobenzylated products have a much lower partition coefficient between the aqueous and the organic phase than have the starting diols. The resulting, lower concentration of the alcoholate anions of the monobenzylated products in the aqueous layer means that dibenzylation will proceed at a much lower rate than monobenzylation. The solvent system used was dichloromethane-water, and the base was tetrabutylammonium hydroxide.

The results obtained for three hexoside diols are shown in Table I. The total

TABLE I

Starting material	Ether product	Yield (%)	M.p. (degrees)		Ref.
Methyl 4,6-O-benzylidene- -α-D-glucopyranoside	2,3-dibenzyl	6	85- 86	-32	5,7
	2-benzyl	54	131-132	+35	5
	3-benzyl	20	187-188	+78	5,6
Methyl 4,6-O-benzylidene- -β-D-glucopyranoside	2,3-dibenzyl	7	118-120	-38	8
	2-benzyl	50	124-125	-27	8
	3-benzyl	20	184-185	48	8
Methyl 2,3-di-O-benzyl- -&-D-glucopyranoside	2,3,4-tribenzyl	18	53- 54	+22.5	9
	2,3,6-tribenzyl	68	Syrup	+11	10

PARTIAL BENZYLATIONS^a

^a100 MHz spectra were in agreement with the postulated structures. ^bIn chloroform.

yields of monobenzyl ethers ranged from 70 to 86%; only small proportions of dibenzyl ethers were produced. Although product analysis at several levels of substitution is required in order to evaluate relative reaction rate constants^{1,3}, the results point to a higher reactivity at the 2-position relative to that at the 3-position, probably because of the higher acidity² of OH-2, as well as to steric control in the preferential benzylation at the primary position in the 4,6-diol.

The following represents a typical preparation (see Ref. 4 for general methods). Methyl 4,6-O-benzylidene- α -D-glucopyranoside (1.00 g, 3.5 mmol), tetrabutylammonium hydrogen sulfate (0.24 g, 0.7 mmol), and benzyl bromide (0.72 ml, 6.0 mmol) were dissolved in dichloromethane (60 ml). Aqueous sodium hydroxide (5 ml of a 5% solution) was added and the mixture boiled under reflux for 48 h. The reaction was monitored by t.l.c. The mixture was cooled and the two layers were separated. The dichloromethane layer was shaken with water, dried (Na₂SO₄), and concentrated. Column chromatography of the residue on silica gel yielded the products listed in Table I.

Only negligible amounts of products were obtained in the absence of tetrabutylammonium hydrogen sulfate.

ACKNOWLEDGMENTS

We are indebted to Professor Bengt Lindberg for his interest and to the Swedish Natural Science Research Council for financial support.

REFERENCES

- 1 H. M. Spurlin, in E. Ott, H. M. Spurlin, and M. W. Grafflin (Eds.), Cellulose and Cellulose Derivatives, II, High Polymers, Vol. V, Interscience, New York, 1954, IX A.
- 2 P. J. Garegg, Acta Chem. Scand., 17 (1963) 1343-1347.
- 3 A. Brändström, Preparative Ion Pair Extraction: An Introduction to Theory and Practice, Apotekarsocieteten, Stockholm, 1975.
- 4 P. J. Garegg, I. J. Goldstein, and T. Iversen, Acta Chem. Scand., in press.

- 5 J. M. Küstner and I. Dyone, Justus Liebigs Ann. Chem., (1975) 2179-2189.
- 6 H. M. Borén, G. Ekborg, and J. Lönngren, Acta Chem. Scand., 10 (1975) 1085-1088.
- 7 C. M. McCloskey, Advan. Carbohyd. Chem., 12 (1957) 137-156.
- 8 H. B. Borén, P. J. Garegg, L. Kenne, L. Maron, and S. Svensson, Acta Chem. Scand., 26 (1972) 644-652.

÷

- 9 R. Eby and C. Schuerch, Carbohyd. Res., 34 (1974) 79-90.
- 10 J. N. BeMiller and R. E. Wing, Carbohyd. Res., 6 (1968) 197-206.