Carbohydrate Research, 53 (1977) C5–C7

Preliminary communication

Monotosylation 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 September 27th, 1976; accepted for publication, October 12th, 1976)

We recently described the benzylation of diols, *e.g.*, suitably protected glycosides having two free hydroxyl groups, using a phase-transfer procedure[1], to produce monobenzyl ethers in good yields[2]. We now report three examples showing that the method is equally applicable for the monotosylation of diols.

Monotosylates of carbohydrate diols are useful synthetic intermediates, and improved methods for their preparation are of interest. So far, the best results have been obtained using *N*-tosylimidazole[3]. In the phase-transfer procedure described here, the ion-pair $Q^+{}^-OR$ is formed in the aqueous phase and then transferred to the organic phase in the equilibrium

$$Q^+_{aq} + RO^-_{aq} \rightleftharpoons Q^+{}^-OR_{org}.$$

Tosylation proceeds in the organic phase. The monotosylate, once formed, has a lower partition coefficient between the aqueous and the organic phase than does the diol. As the ionization most probably occurs mainly in the aqueous phase, and the resulting ion-pair then is transferred to, and tosylated in, the organic phase, this results in a slow tosylation of the monotosylate. High yields of monotosylates are therefore obtainable. Also, the experimental convenience, inherent in the phase-transfer technique, makes this an attractive alternative to existing methods.

The results obtained are shown in Table I.

As found before in analogous monobenzylations[2], the results indicate a higher reactivity at position 2 than at position 3, probably due to the higher acidity of HO-2. The axial or equatorial disposition of the hydroxyl group may be relatively unimportant, as methyl 4,6-*O*-benzylidene-α-D-mannopyranoside yields the 2-tosylate under the conditions described here, but mainly the 3-tosylate on partial tosylation with toluene-*p*-sulphonyl chloride in pyridine[12]. The regioselectivity seems to be better for the α-D-glycosides than for the β-glycoside. Evaluation of relative rate constants, however, requires full product analysis at several levels of substitution.

TABLE I

PARTIAL TOSYLATIONS[a]

Starting material	*Product*	*Yield (%)*	*M.p. (degrees)*	*$[\alpha]_D$ (degrees)*	*Ref.*
Methyl 4,6-*O*-benzylidene-α-D-glucopyranoside	2-Tosylate	78	157–159	+62	4,5,6
	3-Tosylate	7	167–169	+33	6
Methyl 4,6-*O*-benzylidene-β-D-glucopyranoside	2-Tosylate	55	120–121	–45	7,8,9
	3-Tosylate	31	162–163	–85	7,8,9
	2,3-Ditosylate	7	159–160	–61	7,8,9
Methyl 4,6-*O*-benzylidene-α-D-mannopyranoside	2-Tosylate	95	syrup	+2	10

[a] 100-MHz spectra were in agreement with the postulated structures. [b] In chloroform.

The following is a typical preparative procedure (see Ref. 11). Methyl 4,6-*O*-benzylidene-α-D-mannopyranoside[12] (250 mg, 0.9 mmol), tetrabutylammoniumhydrogen sulphate (60 mg, 0.18 mmol), and toluene-*p*-sulphonyl chloride (253 mg, 1.3 mmol) were dissolved in dichloromethane (25 ml). Aqueous sodium hydroxide (2 ml of a 5% solution) was added, and the mixture stirred for 30 min at room temperature. The reaction was monitored by t.l.c. (toluene–ethyl acetate, 2:1). The two layers were separated, and the dichloromethane layer was shaken with water, dried (Na_2SO_4), and concentrated. T.l.c. (toluene–ethyl acetate, 2:1) of the residue showed the presence of one component only. The n.m.r. spectrum was identical to that of the 2-tosylate.

Methyl 4,6-*O*-benzylidene-α- and β-D-glucopyranoside required a 2-h reaction time and the products were separated by column chromatography on silica gel (toluene–ethyl acetate, 1:1).

Only small amounts of products were obtained in the absence of tetrabutylammoniumhydrogen sulphate.

ACKNOWLEDGMENTS

We thank Professor Bengt Lindberg for his interest, the Swedish Natural Science Research Council for financial support, and Stiftelsen Bengt Lundqvists Minne for a maintenance grant (to T.I.).

REFERENCES

1 A. Brändström, *Preparative Ion Pair Extraction: An Introduction to Theory and Practice*. Apotekarsocieteten, Stockholm, 1975.
2 P. J. Garegg, T. Iversen, and S. Oscarson, *Carbohydr. Res.*, 50 (1976) C12–C14.
3 D. R. Hicks and B. Fraser-Reid, *Synthesis*, (1974) 203.
4 G. J. Robertson and C. F. Griffiths, *J. Chem. Soc.*, (1935) 1193–1201.

5 H. R. Bolliger and D. A. Prins, *Helv. Chim. Acta*, 28 (1945) 465–470.
6 A. Zobacova, V. Hermankova, and J. Jarý, *Collect. Czech. Chem. Commun.*, 35 (1970) 327–333.
7 S. Sturm, O. Luderitz, and O. Westphal, *Justus Liebigs Ann. Chem.*, 696 (1966) 180–193.
8 R. D. Guthrie, A. M. Prior, and S. E. Creasey, *J. Chem. Soc., C*, (1970) 1961–1966.
9 J. Stanek, Jr., and J. Jarý, *Justus Liebigs Ann Chem.*, (1976) 163–173.
10 F. R. Seymour, *Carbohydr. Res.*, 34 (1974) 65–70.
11 P. J. Garegg, I. J. Goldstein, and T. Iversen, *Acta Chem. Scand. B 30* (1976) 876–878.
12 J. G. Buchanan and J. C. P. Schwarz, *J. Chem. Soc.*, (1962) 4770–4777.