Carbohydrate Research, 116 (1983) 162–165
Elsevier Science Publishers B. V., Amsterdam – Printed in The Netherlands

Note

A reinvestigation of glycosidation reactions using 1-thioglycosides as glycosyl donors and thiophilic cations as promoters

PER J. GAREGG, CHRISTINA HENRICHSON, AND THOMAS NORBERG

Department of Organic Chemistry, Arrhenius Laboratory, University of Stockholm, S-106 91 Stockholm (Sweden)

(Received October 1st, 1982, accepted for publication, December 14th, 1982)

1-Thioglycosides have received considerable attention in recent years, mainly because of their ability to induce or competitively inhibit the activity of enzymes. The alkylthio or arylthio group is also an excellent protective group for position 1 of sugars, although it has been little used in oligosaccharide synthesis[1,2]. These groups are stable to most conditions for manipulation of *O*-protective groups, except that of catalytic hydrogenation, and the thioglycosides can be converted into the parent hydroxy compound by silver(I)[3] or mercury(II)[4] ion-promoted hydrolysis without affecting other commonly used protective groups. Furthermore, thioglycosides can be directly converted into glycosyl bromides in high yields by treatment with bromine[5], and this should be an attractive feature in oligosaccharide block-synthesis.

In 1973, Ferrier *et al.* reported[6] direct, mercury(II) sulfate-promoted glycosidation of simple alcohols with fully benzylated phenyl 1-thioglycosides. We now report glycosidation reactions employing phenylmercury triflate[7] as promoter and benzylated or acylated phenyl 1-thio-β-D-gluco- or 1-thio-β-D-galacto-pyranosides as glycosyl donors. Other promoters, such as silver triflate, the copper(I) triflate–benzene complex, or the mercury(II) triflate–dimethyl sulfoxide complex, were found to be less efficient. The results are summarised in Table I, and it can be concluded that the stereochemical outcome of the glycosidations was similar to that obtained by using[8] the corresponding glycosyl bromides and silver triflate promotion. A reaction between the glycosyl acceptor alcohol and the promoter, leading to a complex that is less reactive towards thioglycosides, appears to compete with the desired reaction between the thioglycoside and the promoter. This is the probable reason for the low yields obtained with such simple alcohols as methanol and 8-methoxycarbonyloctanol. With sugar primary alcohols, this competing reaction is of less importance and, with some exceptions, the yields in the glycosidations are good. With sugar secondary alcohols, however, yields were acceptable only when benzylated thioglycosides were used. The reason for the low yields with acylated thioglycosides is not clear. The main products isolated in those examples where no

0008-6215/83/$ 03 00

TABLE I

GLYCOSIDATIONS WITH 1-THIOGLYCOSIDES, USING PHENYLMERCURY TRIFLATE AS PROMOTER

Thioglycoside	*Alcohol*	*Solvent*	*αβ-Ratio*	*Total yield (%)*	*Ref.*
11	**1**	CH_2Cl_2	6:4	85	10
11	**4**	CH_2Cl_2	1:0	39	11
11	**6**	CH_2Cl_2	1:0	72	—
12	**1**	CH_3NO_2–toluene (1:1)	0:1	74	12
12	**5**	CH_3NO_2–toluene (1:1)	—	0	—
13	**1**	CH_2Cl_2	0:1	37	13
14	**1**	CH_2Cl_2	8:9	69	14
14	**6**	CH_2Cl_2	9:1	68	—
15	**1**	CH_3NO_2–toluene (1:1)	0:1	67	12
15	**2**	CH_3NO_2–toluene (1:1)	0:1	78	15
15	**3**	CH_2Cl_2	0:1	91	15
15	**7**	CH_2Cl_2	—	0	—
15	**8**	CH_2Cl_2	—	0	—
15	**9**	CH_2Cl_2	—	0	—
15	**10**	CH_2Cl_2	0:1	<10	—
16	**1**	CH_3NO_2–toluene (1:1)	—	0	—

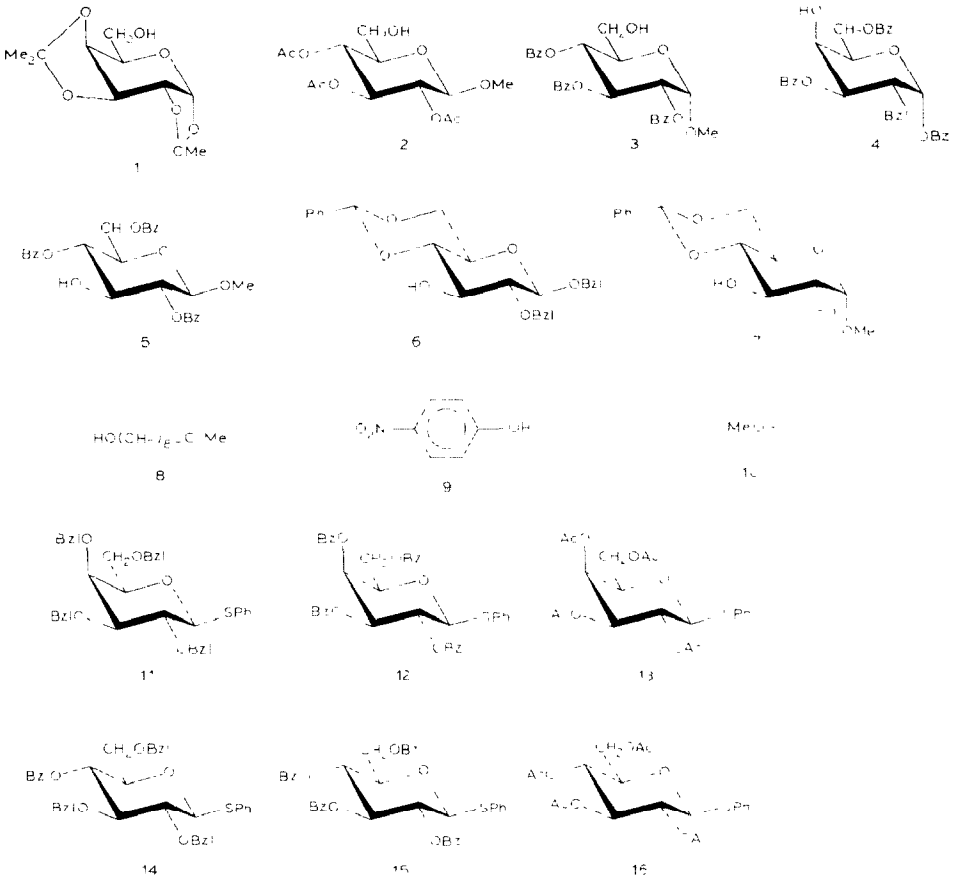
glycosidation was observed were the 1-hydroxy compounds derived from the thioglycosides, even when strictly anhydrous conditions were maintained during glycosidation.

EXPERIMENTAL

The general methods were the same as those previously reported[9].

Phenylmercury trifluoromethanesulfonate[7]. — A mixture of mercury(II) oxide (3.0 g, 13.8 mmol), trifluoromethanesulfonic anhydride (2.1 mL, 12.8 mmol), and dry benzene (60 mL) was heated under reflux until most of the oxide had dissolved. The hot solution was filtered and then cooled to give the crystalline title compound (4.5 g, 76%). The ^{13}C-n.m.r. data were identical to those previously reported[7].

General glycosidation procedure. — A suspension of phenylmercury triflate (1.3 mmol) in solvent (5 mL) was added to a solution of the thioglycoside (1.1 mmol) and the alcohol (1.0 mmol) in solvent (5 mL) containing powdered 4Å molecular sieves. The mixture was stirred at room temperature until t.l.c. indicated reaction to be complete (10–60 min). Pyridine (0.2 mL) was added and the mixture was filtered. The filtrate was diluted with more solvent, washed with 5% aqueous EDTA and aqueous sodium hydrogencarbonate, dried, and concentrated. The re-



sidue was purified by chromatography on silica gel, using a suitable toluene–ethyl acetate mixture for elution. The yields and solvents used are reported in Table I. When an anomeric mixture of glycosides was obtained, the ratio of the anomers was assessed from n.m.r. data.

Characterisation of the products. — Most disaccharides prepared were known compounds and were identified by comparing their n.m.r. spectra and melting points with those of authentic samples. Benzyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-(tetra-*O*-benzyl-α-D-galactopyranosyl)-β-D-glucopyranoside (**17**) and the corresponding *gluco* derivative (**18**) are new compounds, and the physical constants are therefore reported below.

Compound **17**, m.p. 110–111°, $[\alpha]_D$ +9° (*c* 0.4, chloroform). ^{13}C-N.m.r. data ($CDCl_3$, 25°): δ 65.67–82.36 (C-2–C-6), 96.40 (C-1′), 101.62, and 103.32 (C-1, acetal C).

Anal. Calc. for $C_{61}H_{62}O_{11}$: C, 75.4; H, 6.44. Found: C, 75.2; H, 6.51.

Compound **18** was difficult to separate from its β isomer, and therefore only spectral data are given. ^{13}C-N.m.r. data ($CDCl_3$, 25°): δ 65.65–82.12 (C-2–C-6), 95.96 (C-1′), 101.86, and 103.18 (C-1, acetal C).

ACKNOWLEDGMENTS

We thank Professor B. Lindberg for his interest, and the Swedish National Research Council for financial support.

REFERENCES

1 S. A. HOLICK, S.-H. LEE CHIU, AND L. ANDERSON, *Carbohydr. Res.*, 50 (1976) 215–225.
2 S. KOTO, T. UCHIDA, AND S. ZEN, *Bull. Chem. Soc. Jpn.*, 46 (1973) 2520–2523.
3 P. J. GAREGG, H. HULTBERG, AND C. LINDBERG, *Carbohydr. Res.*, 83 (1980) 157–162.
4 D. HORTON AND D. H. HUTSON, *Adv. Carbohydr. Chem.*, 18 (1963) 123–200.
5 F. WEYGAND AND H. ZIEMANN, *Justus Liebigs Ann. Chem.*, 657 (1962) 179–198.
6 R. J. FERRIER, R. W. HAY, AND N. VETHAVIYASAR, *Carbohydr. Res.*, 27 (1973) 55–61.
7 P. PERINGER AND P.-P. WINKLER, *J. Organomet. Chem.*, 195 (1980) 249–252.
8 H. HULTBERG, T. NORBERG, AND J. WALDING, unpublished results.
9 M. FORSGREN AND T. NORBERG, *Carbohydr. Res.*, 116 (1983) 39–47.
10 P. J. GAREGG, C. ORTEGA, AND B. SAMUELSSON, *Acta Chem. Scand., Ser. B*, 35 (1981) 631–633.
11 P. J. GAREGG AND H. HULTBERG, *Carbohydr. Res.*, 110 (1982) 261–266.
12 P. J. GAREGG AND T. NORBERG, *Acta Chem. Scand., Ser. B*, 33 (1979) 116–118.
13 P. J. GAREGG, R. JOHANSSON, AND B. SAMUELSSON, *Acta Chem. Scand., Ser. B*, 36 (1982) 249–250.
14 R. U. LEMIEUX, K. B. HENDRIKS, R. V. STICK, AND K. JAMES, *J. Am. Chem. Soc.*, 97 (1975) 4056–4062.
15 H. BREDERECK, A. WAGNER, D. GEISSEL, P. GROSS, U. HUTTEN, AND H. OTT, *Chem. Ber.*, 34 (1962) 3056–3063.