Carbohydrate Research, 208 (1990) 287–288
Elsevier Science Publishers B.V., Amsterdam

Note

A one-step synthesis of 6-*S*-acetyl-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-thio-α-D-galactopyranose

Mark von Itzstein*, Margot J. Jenkins, and Mauro Mocerino
Department of Pharmaceutical Chemistry, Victorian College of Pharmacy, 381 Royal Parade, Parkville, Victoria 3052 (Australia)

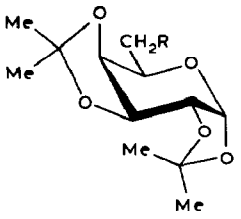
(Received June 4th, 1990; accepted July 16th, 1990)

As part of our interest in thioglycosides of sialic acids, we required 6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-thio-α-D-galactopyranose, which is easily obtained from the 6-thioacetate derivative **1**. Thioacetate **1** has been prepared by Cox and Owen[1] in two steps from the parent alcohol, 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**2**), *via* the 6-*O*-tosyl derivative **3**, with subsequent displacement of tosylate by thioacetate in *N*,*N*-dimethylformamide (DMF) at 100°. The use of the less convenient solvent, DMF, was avoided by converting the tosylate **3** into the iodo sugar **4**, which was subsequently transformed into the required thioacetate **1** by treatment with potassium thioacetate in boiling acetone[1]. Although reasonable yields (>70%) were obtained, both processes suffer in that they are multi-step, the former, having the added disadvantage of requiring the use of DMF.

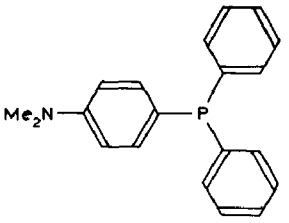
An alternative, one-pot procedure involves the use of the Mitsunobu reaction[2]. Previous work from this laboratory[3] and others[4] has shown that this reaction provides a very mild and selective means of esterifying primary and secondary hydroxyl groups. Indeed, the thioacetalization of the primary hydroxyl groups of sucrose under typical Mitsunobu conditions, in which triphenylphosphine (TPP) and diethyl azodicarboxylate were used, has been reported[5]. Treatment of the alcohol **2** with thioacetic acid in the presence of TPP and diisopropyl azodicarboxylate (DIAD) gave a residue which contained the desired thioacetate **1** along with the byproducts, triphenylphosphine oxide and diisopropyl hydrazinedicarboxylate ($DIADH_2$). Although >90% conversion is achieved in going from **2** to **1** under these conditions, isolation of the desired thioacetate **1** from the reaction byproducts, in particular the phosphine oxide, is tedious, and, more importantly, the overall isolated yield is substantially reduced. We have recently reported[3] that this problem in general can be circumvented by using (*p*-dimethylaminophenyl)diphenylphosphine[6] (**5**) as a replacement for TPP in the Mitsunobu reaction. The phosphine oxide produced is easily removed by an acid wash during work-up, thus allowing the isolation of pure thioacetate **1** in good yield (80%).

* Author for correspondence.

0008-6215/90/$ 03.50



1 R = SAc
2 R = OH
3 R = OTs
4 R = I



5

EXPERIMENTAL

General. — General experimental details have been previously[3] given.

6-S-*Acetyl-6-deoxy-1,2:3,4-di*-O-*isopropylidene-6-thio*-α-D-*galactopyranose* (**1**). — DIAD (0.34 mL, 1.7 mmol) was added to a solution of the phosphine **5** (510 mg, 1.7 mmol) and the alcohol **2** (360 mg, 1.4 mmol) in THF (10 mL) with stirring at −10° under nitrogen. To this solution was added thioacetic acid (0.10 mL, 1.4 mmol), and the reaction was then allowed to warm to room temperature. Upon completion of the reaction (< 30 min by t.l.c.), the solvent was removed, the residue was taken up in ether (75 mL), cooled (−10°), and the insoluble material was removed. The cold filtrate was washed with cold dilute HCl (2 × 25 mL), saturated aq. sodium hydrogencarbonate, and brine, dried, and concentrated. Chromatography (2:8 EtOAc–hexane) afforded the required thioacetate **1** (320 mg, 80%): $[\alpha]_D$ −15.2° (*c* 1.8, $CHCl_3$; lit.[1] −15°). ^{1}H-N.m.r. data (300 MHz): δ 1.32, 1.35, 1.45, and 1.48 (4s, 12 H, CMe_2), 2.34 (s, Ac), 3.04 (part of ABX, $J_{5,6}$ 8.7, $J_{6,6}$ 13.8 Hz, H-6), 3.16 (B of ABX, $J_{5,6}$ 5.0, H-6), 3.85 (ddd, $J_{4,5}$ 1.8 Hz, H-5), 4.24–4.31 (m, 2 H, H-2,H-4), 4.61 (dd, $J_{2,3}$ 7.9, $J_{3,4}$ 2.5 Hz, H-3), and 5.51 (d, $J_{1,2}$ 5.0 Hz, H-1). ^{13}C-n.m.r. data (75.5 MHz): δ 24.5, 25.0, and 26.0 (4 C, CMe_2), 29.7 (C-6), 30.5 (*Me*CO), 66.9, 70.6, 71.0, and 72.1 (C-2–C-5), 96.6 (C-1), 108.8 and 109.5 (CMe_2), and 195.7 (C=O).

ACKNOWLEDGMENTS

We gratefully acknowledge the financial support of the NH and MRC.

REFERENCES

1 J. M. Cox and L. N. Owen, *J. Chem. Soc., C*, (1967) 1121–1130.
2 O. Mitsunobu, *Synthesis*, (1981) 1–28.
3 M. von Itzstein and M. Mocerino, *Synth. Commun.*, 20 (1990) in press.
4 R. P. Volante, *Tetrahedron Lett.*, 22 (1981) 3119–3122.
5 I. D. Jenkins and S. Thang, *Aust. J. Chem.*, 37 (1984) 1925–1930.
6 H. A. Brune, M. Falck, R. Hemmer, G. Schmidtberg, and H. G. Alt, *Chem. Ber.*, 117 (1984) 2791–2802.