Carbohydrate Research, 208 (1990) 264–266
Elsevier Science Publishers B.V., Amsterdam

Note

A simple and ready internal *C*-glycosylation of 2,3,5-tri-*O*-benzylglycofuranoses promoted by the boron trifluoride–diethyl ether complex

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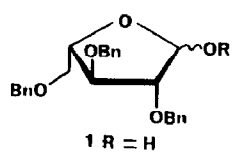
(Received February 1st, 1990; accepted in revised form, May 1st 1990)

Readily available 2,3,5-tri-*O*-benzyl-L-arabinofuranose (**1**), 2,3,5-tri-*O*-benzyl-D-ribofuranose (**4**), their methyl glycofuranosides **2** and **5**, and the corresponding 1-*O*-acetyl compounds **3** and **6** were each treated with boron trifluoride–diethyl ether complex in dichloromethane at room temperature in order to obtain in high yields the (2*S*, 3*S*, 3a*S*, 9b*R*)-3-benzyloxy-2-benzyloxymethyl-3,3a,5,9b-tetrahydro-2*H*-furo[3,2-*c*][2]benzopyran (**7**) and (2*R*, 3*R*, 3a*S*, 9b*R*)-3-benzyloxy-2-benzyloxymethyl-3,3a,5,9b-tetrahydro-2*H*-furo[3,2-*c*][2]benzopyran (**8**).



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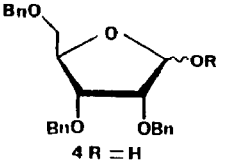
3 R = Ac



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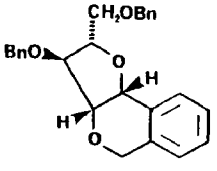

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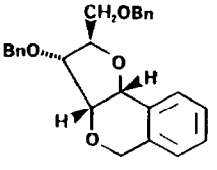

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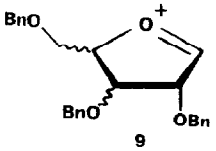

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0008-6215/90/$ 03.50

Numerous papers have recently appeared by Martin and co-workers concerning an interesting intramolecular *C*-arylation of benzylated sugars promoted by tin(IV) chloride[1-4]. The reaction leads to the formation of a carbon–carbon bond between the anomeric centre and the phenyl ring of the 2-*O*-benzyl substituent to give the isochromanes **7** and **8**, which may be synthetic intermediates for the synthesis of naturally occuring compounds[5].

Examination of these papers[1-4] suggested that a particular functionalisation of the anomeric carbon is required for the reaction to proceed efficiently. In fact, using the same Lewis acid [tin(IV) chloride], methyl glycofuranosides **2** and **5** afforded the isomeric isochromanes **7** and **8**, respectively, in only 30% yields, while the corresponding acetates **3** and **6** afforded the same isochroman derivatives in about 60% yield[1-3]. Only 2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl fluoride (obtained laboriously in three steps from the corresponding tri-*O*-benzyl-D-ribofuranose) afforded the isochroman **8** in high yield (83%) in the presence of the boron trifluoride–diethyl ether complex.

Since the mechanism of *C*-arylation should involve the intermediary formation of an oxonium ion such as **9**, we thought that it was of interest to test various Lewis acids in order to improve the effectiveness of the *C*-arylation, which should occur in good yields starting with unfunctionalized furanosides such as **1**, which have not been previously evalutated. In fact, reaction of the tri-*O*-benzylated furanosides **1** and **4** with a series of Lewis acids ($SnCl_4$, $TiCl_4$, $AlCl_3$, $FeCl_3$, $BF_3 \cdot Et_2O$) afforded compounds **7** and **8** in varying yields. The best results were obtained in the reaction with the boron trifluoride–diethyl ether complex, which appeared to be the best promoter for the *C*-arylation.

Treatment of tribenzylated furanosides **1** and **4** with the boron trifluoride–diethyl ether complex in dichloromethane at room temperature afforded compounds **7** and **8** in 95 and 80% isolated yields, respectively. (See General Procedure in Experimental section and Table I).

Under the same conditions, the corresponding methyl glycosides **2** and **5** and the acetates **3** and **6**, which in the reaction with tin(IV) chloride were poor substrates[1-3], afforded the compounds **7** and **8** in similar high yields.

TABLE I

Reaction times, yields, and physicochemical data for products of C-glycosylation

Starting Compound.[a]	*Product*	*Time, min*	*Yields, %*	$[\alpha]_D^{20}$, *deg.*	*(Lit.* $[\alpha]_D$, *deg.)*	*m.p. (Lit. m.p.) deg.*
1	**7**[b]	15	95	−7.3	(−5.4[c])	oil; (oil)[c]
2	**7**	15	95	−7.4		oil
3	**7**	15	96	−7.5		oil
4	**8**[b]	90	80	+74	(+80.5)[e]	111–112°[d] (110–111°)[e]
5	**8**	90	83	+76		111–112°
6	**8**	90	81	+74		111–112°

[a] Prepared according to ref. 8. [b] All other physicochemical and spectral (i.r. m.s., and n.m.r.) properties are identical with those reported[3,5]. Satisfactory elemental analyses (± 0.3%) were obtained for all compounds. [c] See ref. 3. [d] From bis (2-propyl) ether–dichloromethane. [e] See ref. 5.

These results are of interest since they show that, in order to accomplish the internal *C*-arylation, it is not necessary to activate the anomeric carbon atom of **1** and **4** as an acetate or as the fluoride. Thus one can avoid the preparation of these intermediates which require two or three steps from their corresponding methyl derivatives[5–7].

EXPERIMENTAL

General methods. — All m.p.s. are uncorrected. I.r. spectra were measured with a Perkin–Elmer 1420 spectrometer. ^{1}H-n.m.r. spectra were recorded with a Bruker AM-500 instrument for solutions in $CDCl_3$. ^{13}C-n.m.r. spectra were recorded with a Bruker AC-200 instrument for solutions in $CDCl_3$. Optical rotations were measured for $CHCl_3$ solutions. The progress of all reactions was monitored by t.l.c. on Silica Gel HF_{254} (E. Merck) microplates. A 7:3 hexane–ethyl acetate mixture was used as developing solvent for t.l.c., and spots were detected by spraying with 70% sulphuric acid, followed by heating. Mass spectra were recorded on a Varian 112-S mass spectrometer (direct inlet).

General procedure for internal C*-glycosylation.* — [For details (reaction times, yields, etc.), see Table I] The appropriate tribenzylated D-ribo- or L-arabino-furanose (1 mequiv.) was dissolved in dichloromethane (15 mL), and boron trifluoride–diethyl ether complex (3 mequiv.) was added at room temperature. The reaction was completed after 15 min for tribenzylated arabinofuranose **1**, its methyl glycoside **2**, and 1-*O*-acetylderivative **3**. The same reaction was complete after 1.5 h for the tribenzylated ribofuranose **4**, and the corresponding derivatives **5** and **6**. At the appropriate time, the solution was poured into saturated aqueous $NaHCO_3$, extracted with dichloromethane, dried (Na_2SO_4), and evaporated to afford the tetrahydrofurobenzopyrans **7** or **8**.

ACKNOWLEDGMENTS

This work was supported by Ministero della Pubblica Istruzione (M.P.I.).

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