Tetrahedron Letters,Vol.26,No.17,pp 2055-2058,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

THE UNEXPECTED INTRAMOLECULAR C-ARYLATION OF 2-O-BENZYLATED CYCLIC SUGAR DERIVATIVES: A USEFUL 1,2-CIS-C-GLYCOSYLATION REACTION

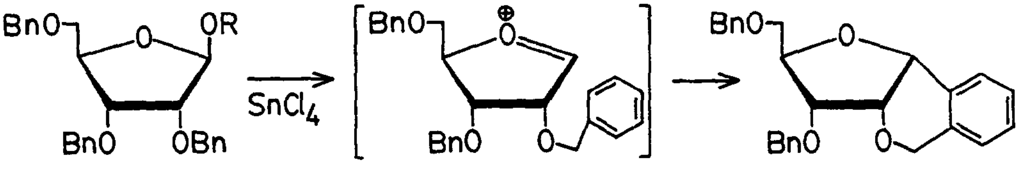
O. R. Martin

Department of Chemistry, State University of New York at Binghamton,
Binghamton, New York 13901, USA

Summary: Upon treatment with tin(IV) chloride, perbenzylated glycofuranosyl acetates such as **3** or **6** undergo an unusual, intramolecular α-C-arylation resulting from the internal Friedel-Crafts alkylation of the 2-O-benzyl substituent.

Per-O-benzylated glycofuranosyl acetates such as **3**, or the corresponding methyl glycoside **1**, are useful starting materials for the synthesis of O- and C-glycosides [1,2], owing, in particular, to the stability and ease of removal of the benzyl protecting groups. However, in the course of our studies on the C-glycosidation of carbohydrate derivatives with functionalized ketene acetals, we have discovered that these benzylated glycofuransosyl acetates are prone to an easy intramolecular reaction, in the presence of a Lewis acid, leading to the creation of a carbon-carbon bond between the anomeric center and the phenyl ring of the 2-O-benzyl substituent. We wish to report, in this communication, the first results of our investigations on this reaction.

Treatment of tri-O-benzyl-β-D-ribofuranosyl acetate **3**[3], prepared by acetylation of **2**[4], with tin(IV) chloride (1 equivalent) in methylene chloride at room temperature (2h) afforded a crystalline product, **5**[5,6], in fair yield (46% after chromatographic separation and crystallization). This compound, which has a chromatographic mobility almost identical to that of the starting material, is characterized by the absence of hydroxyl and carbonyl absorptions on its infrared spectrum, and by a molecular ion peak at m/z 402 on its mass spectrum: this indicates a composition ($C_{26}H_{26}O_4$) corresponding to the loss of a molecule of acetic acid from the starting material, **3**. However, owing to the absence of C=C absorption on its infrared spectrum, as well as to its inertness toward permanganate oxidation, compound **5** does not have the structure of the furanoid glycal derived from **3**: this unsaturated derivative, namely 1,4-anhydro-2,3,5-tri-O-benzyl-D-erythro-pent-1-enitol, has indeed properties [7,8] completely different from those of **5**. As shown by its p.m.r. spectrum, compound **5** contains only 14 aromatic protons and lacks a normal anomeric proton: these features can be explained only by the existence of a carbon-carbon bond between the anomeric carbon and the nearest phenyl group. In view of the conditions of the reaction and the nature of the molecular system, the creation of such a bond is entirely justified: activation of the acetoxy group of the starting material by the Lewis acid may lead indeed to an intermediate oxonium ion such as **4**, which, in absence of external nucleophile, can readily rearrange into **5** by an intramolecular Friedel-Crafts-type alkylation of the 2-O-benzyl group.



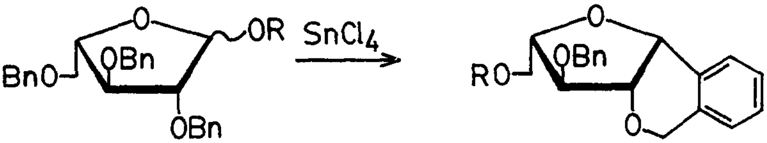
1 R=Me
2 R=H (αβ mixture)
3 R=Ac

4

5

Interestingly, compound **5** has already been mentioned in the literature, with, however, an incorrect structure: according to Winkley [9], the reaction of tri-O-benzyl-D-ribofuranosyl bromide with mercuric cyanide gives, as by-product, a compound having physical properties (only m.p. and m.s. data reported) identical to those of **5**; the structure of this compound, tentatively identified as the dehydrobromination product (furanoid glycal), should therefore be revised.

Under identical conditions, tri-O-benzyl-L-arabinofuranosyl acetate **7**[10] (3:1 α/β ratio), prepared by acetylation of commercially available **6**, was converted into annulated C-glycoside 8[11] as major product (60%) as well as into partially debenzylated derivative 9[12] (21%, isolated yields). These results demonstrate the high overall yield of the intramolecular C-arylation reaction.



6 R=H
7 R=Ac

8 R=Bn
9 R=H

In the hexopyranoid series, treatment of tetra-O-benzyl-α-D-glucopyranosyl acetate[13], prepared from commercially available tetra-O-benzyl-D-glucopyranose, under similar conditions, gave a complex mixture from which a compound (m.p. 72-75°) has been isolated in low yield. This compound has undoubtedly the structure of an intramolecular C-arylation product, but needs further investigation. The complexity of the mixture seems to be due primarily to the partial debenzylation of the final product(s).

These unexpected results thus demonstrate the high reactivity of the 2-O-benzyl substituent of perbenzylated carbohydrate derivatives under Lewis acid-catalyzed O- and C-glycosylation conditions. As the first examples of participation of benzyl groups in reactions at the anomeric center, these C-arylations provide a novel, simple methodology for stereospecific 1,2-cis-C-glycosylation. Furthermore, they give ready access to complex isochroman derivatives, a heterocyclic system for which very few synthetic methods are available. Further elaboration of the polyheterocycles and extension to substituted benzyl groups are currently under active investigation and the results will be reported shortly.

Acknowledgement is made to the Donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the Research Foundation of SUNY-Binghamton, for support of this research.

References and notes

1. T. Mukaiyama, S. Kobayashi, and S. Shoda, Chem. Lett., 907 and 1529 (1984).
2. M. T. Reetz and H. Müller-Starke, Liebigs Ann. Chem., 1726 (1983).
3. O. Makabe, M. Nakamura, and S. Umezawa, Bull. Chem. Soc. Jpn., 48, 3210 (1975).
4. R. Barker and H. G. Fletcher, Jr., J. Org. Chem., 26, 4605 (1961).
5. All new products gave satisfactory microanalytical results and spectral properties.
6. m.p. 111-112°C (from chloroform-ether-hexane); $[\alpha]_D^{20}$ +79.8° (c 0.87, $CHCl_3$).
7. E. Zissis and C. P. J. Glaudemans, Carbohydr. Res., 50, 292 (1976).
8. J. G. Buchanan, A. R. Edgar, M. J. Power, and G. C. Williams, Carbohydr. Res., 55, 225 (1977).
9. M. W. Winkley, Carbohydr. Res., 31, 245 (1973).
10. O. Makabe, J. Yajima, and S. Umezawa, Bull. Chem. Soc. Jpn., 49, 3552 (1976).
11. Syrup; $[\alpha]_D^{20}$ -5.4° (c 1.1, $CHCl_3$).
12. m.p. 72-73°; $[\alpha]_D^{20}$ -51.4° (C 0.53, $CHCl_3$).
13. R. U. Lemieux, K. B. Hendriks, R. V. Stick, and K. James, J. Am. Chem. Soc., 97, 4056 (1975).

(Received in USA 11 February 1985)