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STRUCTURAL ELUCIDATION AND A NOVEL REDUCTIVE CLEAVAGE OF RIBOFURANOSYL RING C-1 - O BOND OF THE INTRAMOLECULAR C-ARYLATION PRODUCT OF TRI-O-BENZYL-β-D-RIBOFURANOSYL FLUORIDE

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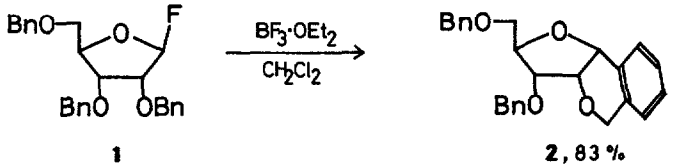
Abstract: Treatment of 2,3,5-tri-O-benzyl-β-D-ribofuranosyl fluoride (**1**) with $BF_3 \cdot OEt_2$ in CH_2Cl_2 gave the intramolecular C-arylation product (**2**) formed from the reaction with the 2-O-benzyl group in a 83% yield. Catalytic transfer hydrogenolysis of **2** using HCOOH as a hydrogen donor and the following acetylation of the product gave (3S,1'S,2'R)-3-(1,2,3-triacetoxypropyl)isochroman (**9**) in a 68% total yield.

We have briefly announced a novel intramolecular C-arylation reaction of 2,3,5-tri-O-benzyl-β-D-ribofuranosyl fluoride (**1**).[2] It was, however, difficult to determine the structure of the product from its ^{1}H- and ^{13}C-nmr spectra, so several related reactions and debenzylation reactions were examined to provide structural proofs. During continued investigation, O. R. Martin reported that the same product was formed on the treatment of 1-O-acetyl-2,3,5-tri-O-benzyl-β-D-ribofuranose with $SnCl_4$.[3] He proposed the structure **2** for the product,[3] and later, in his full length paper,[4] the ^{1}H- and ^{13}C-nmr spectra were discussed as structural evidence. In this communication we provide unequivocal structural determination of **2** in agreement with his proposal, and also a new type of the cleavage reaction of ribofuranosyl ring C-1 - O bond will be described.

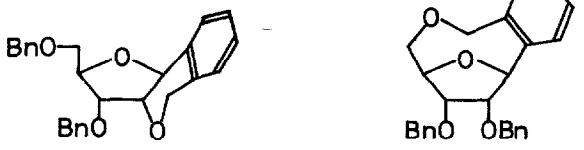
Treatment of **1**[5,6] with $BF_3 \cdot OEt_2$ (0.5 eq) in CH_2Cl_2 at room temperature for 20 min gave 2',1''-anhydro-1-(3,5-di-O-benzyl-α-D-ribofuranosyl)-2-hydroxymethylbenzene (**2**)[7] in a 83% yield. The melting point,[8] the specific rotation,[8] and the ^{13}C-nmr spectrum of **2** were identical with those of Martin's material,[4] but all the chemical shifts of ^{1}H-nmr spectrum of ours[8] were at lower field by ca. 0.08 ppm than those of the corresponding signals of Martin's,[4] while the coupling patterns of both spectra were identical; this discrepancy may be due to his misreadings of the chemical shifts (we repeated several times measurement of the ^{1}H-nmr spectrum of **2** and determination of the chemical shifts of the signals).

For the intramolecular C-arylation there are three possible C - C bond formations; C-glycosylation with the 2-O-benzyl group through α-linkage (**2**), through β-linkage (**3**), and with the 5-O-benzyl group through β-linkage (**4**). In accordance with Martin's indication[4] the coupling pattern of the ribofura-

nose ring protons of **2** is close to $^{3}\underline{T}_{2}$ conformation of the ring and thus agree well with the structure **2**. The structure **3** has a very rigid bicyclic system, in which the ribofuranose ring is fixed as $^{2}\underline{E}$ conformation, and therefore is ruled out. The structure **4**, however, has a very flexible bicyclic system, in which the ribofuranose ring easily pseudorotates between $^{3}\underline{T}_{2}$ and $^{2}\underline{T}_{3}$ conformations. A little distorted $^{3}\underline{T}_{2}$ conformation or the $^{3}\underline{T}_{2}$ conformation equilibrated with some extent of $^{2}\underline{T}_{3}$ conformation could agree with the coupling pattern including the couplings between H-4' and H-5'A, and H-4' and H-5'B. Thus we could not completely exclude the possibility of the structure **4**.

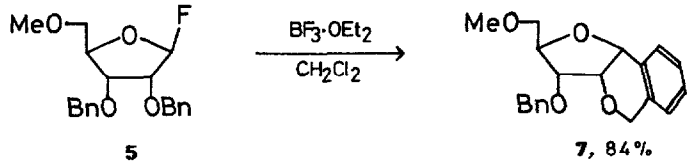


1 **2**, 83 %

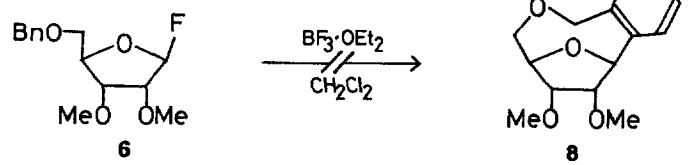


3 **4**

In order to determine which is the real structre of the two, we tried the similar intramolecular C-arylation reactions of 2,3-di-O-benzyl-5-O-methyl-β-D-ribofuranosyl fluoride (**5**)[9] and 5-O-benzyl-2,3-di-O-methyl-β-D-ribofuranosyl fluoride (**6**).[9] Compound **5** readily gave the corresponding intramolecular C-arylation product **7** in a 84% yield, whereas **6** did mostly decomposed materials and the corresponding intramolecular C-arylation product **8** was not isolated. The ^{1}H-nmr spectrum of **7**[10] has essentially the same pattern as that of **2** except for the parts of 5-O-methyl group. Thus the structure of the intramolecular C-arylation product of **1** was deduced as the structure **2**.



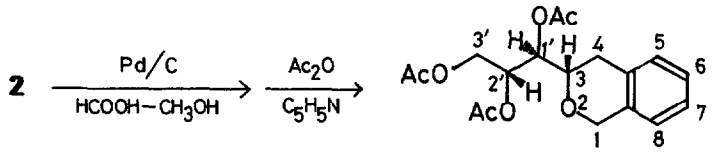
5 **7**, 84%



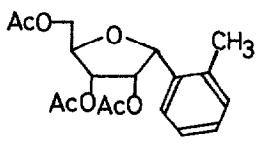
6 **8**

Furthermore, to establish synthetic utilities of this unique C-arylation reaction as well as to obtain more direct structural proofs, catalytic debenzylation of **2** was examined. Several attempts to hydrogenolyze **2** with atmospheric pressure hydrogen in the presence of Pd/C even for four weeks or longer

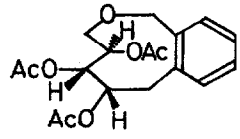
gave no homogeneous product but complex mixtures (monitering by tlc). On the other hand, catalytic transfer hydrogenolysis[11] of 2 proceeded very easily. Treatment of 2 with Pd/C in HCOOH - MeOH under nitrogen atmosphere at room temperature for 30 min gave a homogeneous material, which was then acetylated to give (3S,1'S,2'R)-3-(1,2,3-triacetoxypropyl)isochroman (9) in a 68% total



9, 68%



10



11

yield. The ^{1}H-nmr spectrum[12] of 9 clearly distinguishes its structure from the structure 10, and also from the structure 11 which should be considered to be transformed from the structure 4. The spectrum has a C-benzyl methylene signal (2.71 ppm and 2.90 ppm) besides a O-benzyl methylene signal (4.78 ppm and 4.89 ppm) but no toluene-like methyl signal; thus the structure 10 was ruled out. The proton (H-3, 3.89 ppm) vicinal to the C-benzyl methylene protons is on the carbon adjacent to ether-oxygen and the terminal methylene protons (H-3'A and B, 4.28 ppm and 4.44 ppm) are to ester-oxygen; thus the structure 11 was also ruled out. From the isolation of the compound 9 we could unequivocally decide the structure of 2 and at the same time found a new type cleavage reaction of ribofuranosyl ring C-1 - O bond. T. Nakagawa et al.[13] also presented a similar reductive cleavage of glucopyranosyl ring C-1 - O bond of a intramolecular C-arylation product obtained as a by-product in their cyclooligosaccharide synthesis. Their reductive cleavage by Pd/C catalyzed medium pressure hydrogenolysis, however, needed a long reaction time.

Applications of this reductive cleavage reaction to the synthesis of naturally occurring higher-carbon sugars are now in progress.

NOTES AND REFERENCES

1 Present address : Research Institute for Polymers and Textiles, Yatabe-Higashi, Tsukuba, Ibaraki 305, JAPAN.

2 Y. Araki, K. Itoh, F.-H. Kuan, K. Watanabe, N. Kobayashi, and Y. Ishido, 187th ACS National Meeting, St. Louis, Missouri, Apr. 8 - 13, 1984 (Abstr., CARB 29); $BF_3 \cdot OEt_2$ catalyzed reactions of 1 with isopropenyl trimethylsilyl ether, allyltrimethylsilane, and trimethylsilyl cyanide gave the corresponding C-glycosyl compounds, while those with trimethyl-

silyl acetylene and ethyl trimethylsilylacetate gave a intramolecular C-arylation product.

3 O. R. Martin, Tetrahedron Lett., **26**, 2055 - 2058 (1985).

4 O. R. Martin, Carbohydr. Res., **171**, 211 - 222 (1987).

5 Y. Araki, K. Watanabe, F.-H. Kuan, K. Itoh, N. Kobayashi, and Y. Ishido, Carbohydr. Res., **127**, C5 - C9 (1984); F.-H. Kuan, N. Kobayashi, K. Watanabe, K. Itoh, Y. Araki, and Y. Ishido, J. Chem. Soc. Jpn. (Nippon Kagaku Kaishi), 2040 - 2047 (1985); Y. Araki, N. Kobayashi, K. Watanabe, and Y. Ishido, J. Carbohydr. Chem., **4**, 565 - 585 (1985).

6 T. Mukaiyama, Y. Hashimoto, and S. Shoda, Chem. Lett., 935 - 938 (1983).

7 This name is used for convenience to carbohydrate chemists. For the systematic name see ref. 4.

8 M.p. 110 - 111°C; $[\alpha]_D^{27}$ +80.5° (c 1.14, $CHCl_3$); and ^{1}H-nmr (360 MHz, $CDCl_3$ - TMS): δ 3.62 (1H, dd, $J_{4',5'A}$ 3.2Hz, $J_{5'A,5'B}$ 11.0Hz, H-5'A), 3.78 (1H, dd, $J_{4',5'B}$ 2.2Hz, H-5'B), 4.15 (1H, bt, $J_{1',2'}$ 2.6Hz, $J_{2',3'}$ 4.1Hz, H-2'), 4.27 (1H, dbt, $J_{3',4'}$ 8.8Hz, H-4'), 4.34 (1H, dd, H-3'), 4.52 and 4.64 (2×1H, 2×d, AB type, J 12.2Hz, OCH_2Ph), 4.62 and 4.92 (2×1H, 2×d, AB type, J 14.8Hz, OCH_2Ph), 4.62 and 4.77 (2×1H, 2×d, AB type, J 12.3Hz, OCH_2Ph), 4.76 (1H, ∿d overlapped with one proton of OCH_2Ph, H-1'), 7.08 (1H, ∿dd, J ∿3.5Hz and ∿5.3Hz, one of aromatic protones), 7.25 - 7.40 (12H, m, aromatic protons), and 7.45 (1H, ∿dd, J ∿3.8Hz and ∿5.8Hz, one of aromatic protons).

9 Y. Araki, N. Kobayashi, Y. Ishido, and J. Nagasawa, Carbohydr. Res., **171**, 125 - 139 (1987).

10 M.p. 58.5 - 60.1°C; $[\alpha]_D^{22}$ +107.1° (c 1.12, $CHCl_3$); and ^{1}H-nmr (360 MHz, $CDCl_3$ - TMS): δ 3.38 (3H, s, OCH_3), 3.49 (1H, dd, $J_{4',5'A}$ 3.1Hz, $J_{5'A,5'B}$ 10.9Hz, H-5'A), 3.69 (1H, dd, $J_{4',5'B}$ 2.05, H-5'B), 4.16 (1H, t, $J_{1',2'}$ 2.75Hz, $J_{2',3'}$ 3.75Hz, H-2'), 4.23 (1H, ddd, $J_{3',4'}$ 8.95Hz, H-4'), 4.27 (1H, dd, H-3'), 4.61 and 4.92 (2×1H, 2×d, AB type, J 14.8Hz, OCH_2Ph), 4.66 and 4.82 (2×1H, 2×d, AB type, J 12.1Hz, OCH_2Ph), 4.76 (1H, d, H-1'), 7.07 (1H, ∿dd, J ∿3.4Hz and ∿5.0Hz, one of aromatic protones), and 7.25 - 7.47 (8H, m, the other aromatic protones).

11 Recently catalytic transfer hydrogenation was used widely in peptide chemistry and also applied successfully to carbohydrate chemistry. Peptide chemistry: A. M. Felix, E. P. Heimer, T. J. Lambros, C. Tzougraki, and J. Meienhofer, J. Org. Chem., **43**, 4194 - 4196 (1978); K. M. Sivanandaiah and S. Gurusiddappa, J. Chem. Res. (S), 108 - 109 (1979); R. Colombo, J. Chem. Soc., Chem. Commun., 1012 - 1013 (1981); M. K. Anwer and A. F. Spatola, Tetrahedron Lett., **22**, 4369 - 4372 (1981); M. K. Anwer, A. F. Spatola, C. D. Bossinger, E. Flanigan, R. C. Liu, D. B. Olsen, and D. Stevenson, J. Org. Chem., **48**, 3503 - 3507 (1983); H. Paulsen and M. Schultz, Carbohydr. Res., **159**, 37 - 52 (1987). Carbohydrate chemistry: V. S. Rao and A. S. Perlin, Carbohydr. Res., **83**, 175 - 177 (1980); S. Hanessian, T. J. Liak, and B. Vanasse, Synthesis, 396 - 397 (1981); T. Bieg and W. Szeja, Synthesis, 76 - 77 (1985); D. Beaupere, I. Boutbaiba, G. Demailly, and R. Uzan, Carbohydr. Res., **180**, 152 - 155 (1988).

12 Syrup; $[\alpha]_D^{22}$ -27.1° (c 0.72, $CHCl_3$); and ^{1}H-nmr (200 MHz, $CDCl_3$ - TMS): δ 2.07, 2.08, and 2.13 (3×3H, 3×s, 3×$OCOCH_3$), 2.71 (1H, dd, $J_{3,4A}$ 3.5Hz, $J_{4A,4B}$ 15.8Hz, H-4A), 2.90 (1H, dd, $J_{3,4B}$ 10.8Hz, H-4B), 3.89 (1H, ddd, $J_{3,1'}$ 6.4Hz, H-3), 4.28 (1H, dd, $J_{2',3'A}$ 7.3Hz, $J_{3'A,3'B}$ 12.2Hz, H-3'A), 4.44 (1H, dd, $J_{2',3'B}$ 3.2Hz, H-3'B), 4.78 and 4.89 (2×1H, 2×d, AB type, J 15.4Hz, H-1A,B), 5.27 (1H, dd, $J_{1',2'}$ 4.2Hz, H-1'), 5.49 (1H, ddd, H-2'), 6.99 (1H, bt, J ∿3.8 and ∿5.0Hz, one of aromatic protons), and 7.07 - 7.2 (3H, m, the other aromatic protons).

13 T. Nakagawa, R. Kani, and I. Yamagami, 54th Annual Meeting of Chemical Society of Japan, Tokyo, Japan, Apr. 1 - 4, 1987 (Abstr. p.1161).

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