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A FACILE SYNTHESIS OF α-C-RIBOFURANOSIDES FROM 1-O-ACETYL RIBOSE IN THE PRESENCE OF TRITYL PERCHLOLATE

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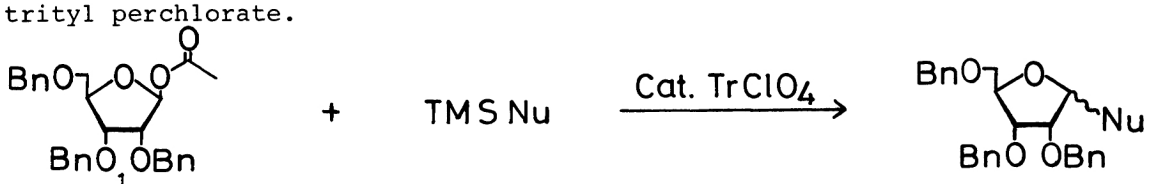
In the presence of a catalytic amount of trityl perchlorate, 1-O-acetyl ribose stereoselectively reacts with silylated nucleophiles, such as silyl enol ether, allylsilane, and trimethylsilyl cyanide, to give the corresponding α-C-ribofuranosides in excellent yields.

Stereoselective synthesis of functionalized C-glycosides is one of the most effective and popular approaches to the preparation of C-nucleosides. Several methods for the synthesis of β-C-ribofuranosides[1] have already been known, however, few general and versatile methods for the synthesis of α-C-ribofuranosides have been reported.[2]

In the previous paper,[3] we have shown that in the presence of trityl perchlorate 1-O-acyl sugars stereoselevtively react with alcohols to give the corresponding α-glycosides in good yields. Herein we wish to describe an equally efficient method for the preparation of α-C-ribofuranosides by the reaction of 1-O-acetyl ribose with silylated nucleophiles in the presence of a catalytic amount of trityl perchlorate.



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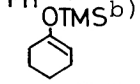
The reaction of 1-O-acetyl-2,3,5-tri-O-benzyl-β-D-ribofuranose (1) with the silyl enol ether of tert-butyl methyl ketone in the presence of a catalytic amount of trityl perchlorate afforded two anomers of 3,3-dimethyl-1-(2,3,5-tri-O-benzyl-D-ribofuranosyl)-2-butanone (93%, 99:1 stereoselectivity): the major anomer (2)[4]: colorless oil, ^{1}H NMR ($CDCl_3$) δ 3.00 (dd), 2.95 (dd) ($-CH_2-$), ^{13}C NMR ($CDCl_3$) δ 214.6 (C=O), 37.3 (C-2), $[\alpha]_D^{25}$+35° (c 1.0, $CHCl_3$); the minor anomer (3)[5]: white crystal, ^{1}H NMR ($CDCl_3$) δ 2.70 (dd), 2.55 (dd) ($-CH_2-$), ^{13}C NMR ($CDCl_3$) δ 213.3 (C=O), δ 40.4 (C-2), $[\alpha]_D^{25}$+27° (c 1.0, $CHCl_3$), mp 30-31 °C. Treatment of 2 with sodium methoxide (under thermodynamic conditions) gave the mixture of 2 and 3 (2:3=42:58) separated by column chromatography on silica gel.

These data, especially based on the most definitive evidence that the chemical shift value of the C-2 carbon atom of 2 is smaller than that of 3,[6] suggested that 2 and 3 could be assigned to the α-anomer and the β-anomer respectively.[7]

Similarly, α-anomers were obtained in excellent yields in the case of the silyl enol ethers derived from acetophenone and cyclohexanone. Also α-anomer was exclusively prepared by employing allyltrimethylsilane as C-nucleophile under the same reaction conditions. The structure of this compound was confirmed by the chemical transformation.[8] Furthermore, α-anomer was obtained almost exclusively by the reaction of 1 with trimethylsilyl cyanide in ether solvent, while anomeric mixtures were afforded under the same reaction conditions in DME. (see Table 1)

A typical procedure is as follow: the mixture of 1 (0.3 mmol), the silyl enol ether of tert-butyl methyl ketone (0.5 mmol), and trityl perchlorate (0.015 mmol) in DME was stirred at 0 °C for 0.5-1 h. The phosphate buffer (pH=7) was added and the reaction mixture was extracted with ether. The organic layer was dried and the solvent was removed under reduced pressure. The residue was chromatographed on silica gel to give 2 (92%) and 3 (1%).

Table 1. Synthesis of α-C-ribofuranosides

Nu	Solvent	Yield/%	α/β	$[\alpha]_D$/°(c, t/°C)[a]
	DME	93	99/1	+35 (1.0, 25)
	DME	97	100/0	+37 (1.1, 24)
	DME	93	96/4	+57 (1.0, 24)[c] / +17 (1.1, 25)
	DME	90	100/0	+48 (1.0, 24)[d]
TMSCN	DME	97	63/37	+73 (1.0, 24)[e]
TMSCN	Et_2O	93	93/7	

a) Optical rotation of α-anomers in $CHCl_3$. b) Two diastereomers were separated. c) Mp 60.5-61.0 °C. d) Mp 55.5-56.0 °C. e) Lit.[9] $[\alpha]_D^{25}$+70° (c 1, $CHCl_3$).

References

1) S. Hanessian and A. G. Pernet, Adv. Carbohydr. Chem. Biochem., 33, 111 (1976).
2) Recently several routes to α-C-ribofuranosides were reported: a) F. Germain, Y. Chapleur, and B. Castro, Tetrahedron, 38, 3593 (1982); b) Y. Araki, K. Watanabe, F-H. Kuan, K. Itoh, N. Kobayashi, and Y. Ishido, Carbohydr. Res., 127, C5 (1984); c) T. L. Cupps, D. S. Wise, and L. B. Townsend, J. Org. Chem., 47, 5115 (1982); d) A. P. Kozikowski and K. L. Sorgi, Tetrahedron Lett., 38, 3593 (1982).
3) T. Mukaiyama, S. Kobayashi, and S. Shoda, Chem. Lett., 1984, 907.
4) Elemental analysis, Found: C, 76.35; H, 7.66%. Calcd for $C_{32}H_{38}O_5$: C, 76.46; H, 7.62%.
5) Elemental analysis, Found: C, 76.44; H, 7.80%.
6) H. Ohrui, G. H. Jones, J. G. Moffatt, M. L. Maddox, A. T. Christensen, and S. K. Byram, J. Am. Chem. Soc., 97, 4602 (1975).
7) Recently, Reetz et al. assigned 2 to β-anomer. M. T. Reetz and H. Müller-Starke, Liebigs Ann. Chem., 1983, 1726. However, in addition to the NMR data, an umbiguous chemical transformation of 2 supported our assignment. Namely, the Bayer-Villiger oxidation of 2 (m-CPBA), followed by hydrolysis of tert-butyl ester (CF_3COOH) gave the corresponding carboxylic acid. Diazomethane treatment afforded the methyl ribofuranosylacetate whose spectral data were in complete agreement with those of α-anomer reported in the literature.[6]
8) Debenzylation (H_2/Pd-C) followed by benzoylation (BzCl/py) afforded O-benzoylated C-riboside which was identical with the sample prepared by hydrogenation of O-benzoylated C-allylated α-riboside. See Ref. 2c ,d .
9) F. G. de las Heras and P. Fernandez-Resa, J. Chem. Soc., Perkin Trans. 1, 1982, 903.

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