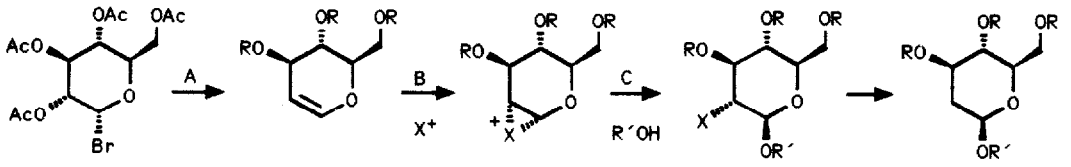
Tetrahedron Letters,Vol.30,No.19,pp 2529-2532,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

AN EASY SYNTHESIS OF 2'-DEOXY-β-DISACCHARIDES[1]

Michel Trumtel, Alain Veyrières and Pierre Sinaÿ*
Ecole Normale Supérieure, Laboratoire de Chimie, UA 1110,
24 Rue Lhomond, 75231 Paris Cedex 05, France

Abstract: 1,2-Di-*O*-acetyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranose and analogs are excellent β-glycosyl donors in the presence of trimethylsilyltriflate. The resulting disaccharides are easily converted into the corresponding 2'-deoxy-β-disaccharides, opening a practical route to this important class of natural molecules.

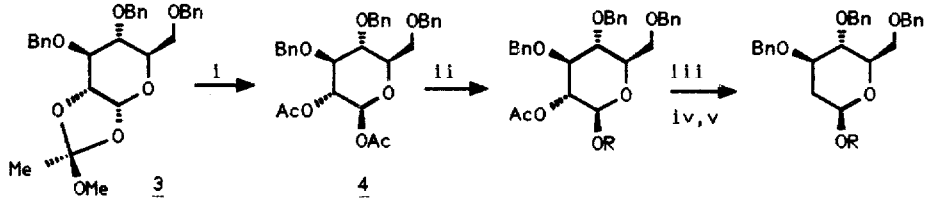
2-Deoxy-β-D-glycosides are sugar components of various natural products, such as the orthosomycin group[2] of antibiotics and a series of cytostatics including chromomycin A_3[3], olivomycin A[4], and mithramycin[5]. Reported methods for the selective preparation of such glycosides often benefit[6] from the directing effect of a temporary neighboring group at C-2, which is subsequently removed under mild conditions, leaving behind the desired 2-deoxy-β-glycoside as shown in the following scheme :



1 2

Analysis of this current circuitous strategy reveals a shortcoming. The initial and appropriate orientation of the participating *O*-acetyl group at C-2 in compound 1 is deliberately lost during the formation of glucal 2 so that the now problematic issue of the glycosylation results from the rather critical stereochemical outcome of steps B and C[7].

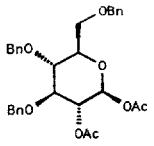
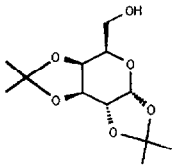
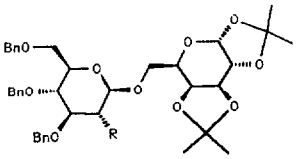
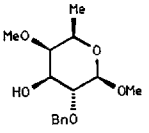
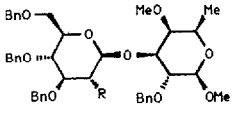
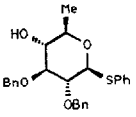
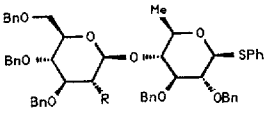
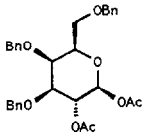
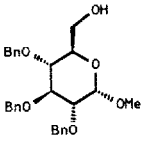
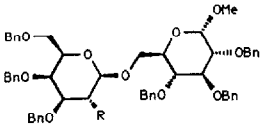
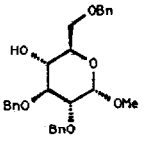
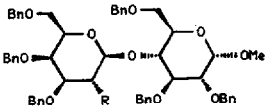
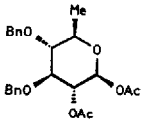
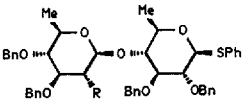
We would like to report on a *fully stereoselective, general and high-yielding synthesis of 2'-deoxy-β-disaccharides*, where the stereochemical outcome is directly governed by the natural orientation of the *O*-acetyl group at C-2 as shown in the following scheme :



3 4

Reagents: *i)* dry CH_3COOH, 1 h, 20°C; *ii)* ROH (1 equiv.),

TABLE 1

GLYCOSYL DONOR	GLYCOSYL ACCEPTOR	DISACCHARIDE[12] (Yield %)
 **4**		 **11** R = OAc (85) → **12** R = H (70)
4	 **7**[19]	 **13** R = OAc (78) → **14** R = H (82)
4	 **8**[21]	 **15** R = OAc (75) → **16** R = H (82)
 **5**	 **9**[23]	 **17** R = OAc (81) → **18** R = H (95)
5	 **10**[24]	 **19** R = OAc (90) → **20** R = H (77)
 **6**	**8**	 **21** R = OAc (80) → **22** R = H (80)

CH_2Cl_2, 4 Å MS, TMSOTf (1 equiv.), 20 min, -20°C; *iii)* MeOH, NaOMe, 1 h, 20°C; *iv*) NaH, imidazole, CS_2, ICH_3, THF, 1 h, 20°C; *v)* Bu_3SnH (10 equiv.), AIBN, toluene, 3 h, reflux[9].

Although easily available benzylated orthoesters were directly used as glycosyl donors[10,11], yields and selectivities were not always high. Known **3**[10] was thus converted into the corresponding 1,2-trans-di-*O*-acetyl derivative **4** (85%)[12]. In the presence of trimethylsilyltriflate[13], **4** was consistently an excellent β-glycosyl donor at -20°C, as shown in Table I, which also includes the results with 1,2-trans-di-*O*-acetyl derivatives **5**[14] and **6**[16].

A somewhat similar approach to the problem has been the selective deoxygenation at C-2' of a natural β-linked disaccharide[18], but the regioselective manipulation of protecting groups in disaccharides is not always straightforward.

In conclusion, the availability of benzylated β-acetates of types **4**, **5** and **6** opens the route to a simple, probably general, efficient and stereospecific preparation of a variety of 2'-deoxy-β-disaccharides. A limitation of this approach lies in the impossibility of using acylated glycosyl acceptors, inasmuch as regiospecific deoxygenation at C-2' would be rather problematic. In order to enlarge the scope of this strategy we thus developed another related approach, whereby the protection of either the glycosyl donor or acceptor with *O*-acyl was made feasible. It is presented in the following letter.

References and notes

1 Part of this work was presented at the 4th European Carbohydrate Symposium, Darmstadt (Germany), A-121, 1987.

2 D.E. Wright, Tetrahedron, 35, 1207 (1979).

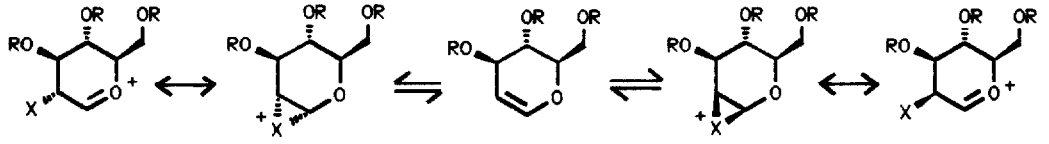
3 M. Miyamoto, Y. Kawamatsu, K. Kawashima, M. Shinohara, K. Tanaka, S. Tatsuoka and K. Nakanishi, Tetrahedron, 23, 421 (1967).

4 Yu.A. Berlin, S.E. Esipov and M.N. Kolosov, Khim. Prir. Soedin., 5, 567 (1969).

5 G.P. Bakhaeva, Yu.A. Berlin, E.F. Boldyreva, O.A. Chuprunova, M.N. Kolosov, V.S. Soifer, T.E. Vasiljeva and I.V. Yartseva, Tetrahedron Lett., 3595 (1968).

6 J. Thiem, M. Gerken and K. Bock, Liebigs Ann. Chem., 462 (1983); K. Bock, I. Lundt and C. Pedersen, Carbohydr. Res., 130, 125 (1984); J. Thiem and M. Gerken, J. Carbohydr. Chem., 1, 229 (1983); K.C. Nicolaou, T. Ladduwahetty, J.L. Randall and A. Chucholowski, J. Am. Chem. Soc., 108, 2466 (1986); R. Preuss and R.R. Schmidt, Synthesis, 694 (1988); M. Perez and J.-M. Beau, Tetrahedron Lett., 75 (1989).

7 The kinetic diastereofacial selective formation of an onium intermediate does not insure the stereoselective formation of the β-glycoside, in that the following equilibration may take place[8]



8 K. Tatsuta, K. Fujimoto, M. Kinoshita and S. Umezawa, Carbohydr. Res.,

54, 85 (1977).
9 D.H.R. Barton and S.W. McCombie, J. Chem. Soc., Perkin Trans. I, 1574 (1975); W. Hartwig, Tetrahedron, 39, 2609 (1983).
10 H.B. Boren, G. Ekborg, K. Eklind, P.J. Garegg, A. Pilotti and C.-G. Swahn, Acta Chem. Scand., 27, 2639 (1973).
11 J.-C. Jacquinet and P. Sinaÿ, Tetrahedron, 32, 1693 (1976).
12 All new compounds gave satisfactory microanalytical and spectral data. Values of $[\alpha]_D$ and δ_H were measured for $CHCl_3$ and $CDCl_3$ solutions, at 20° and 25°C, respectively.
4: $[\alpha]_D$ +25.5°; δ_H: 5.64 (1 H, d, $J_{1,2}$ 8.5 Hz, H-1).
Selected physical data for key disaccharidic compounds:
11: $[\alpha]_D$ -34°; δ_H: 5.54 (1 H, d, $J_{1,2}$ 5.0 Hz, H-1), 4.46 (1 H, d, $J_{1',2'}$ 8.0 Hz, H-1'), 5.03 (1 H, dd, $J_{2',3'}$ 9.0 Hz, H-2').
12: $[\alpha]_D$ -47°; δ_H: 5.61 (1 H, d, $J_{1,2}$ 5.0 Hz, H-1), 4.54 (1 H, dd, $J_{1',2'eq}$ 2.0, $J_{1',2'ax}$ 9.5 Hz, H-1').
13: m.p. 136°C (ethanol), $[\alpha]_D$ +12°; δ_H: 5.01 (1 H, d, $J_{1',2'}$ 8.0 Hz, H-1'), 4.17 (1 H, d, $J_{1,2}$ 7.5 Hz, H-1).
14: m.p. 95°C (CH_2Cl_2-hexane), $[\alpha]_D$ +2°; δ_H: 4.68 (1 H, dd, $J_{1',2'eq}$ 2.0, $J_{1',2'ax}$ 10 Hz, H-1'), 4.22 (1 H, d, $J_{1,2}$ 7.5 Hz, H-1).
15: m.p. 129-130°C (ethanol), $[\alpha]_D$ +22°; δ_H: 5.04 (1 H, dd, $J_{1',2'}$ 8.5, $J_{2',3'}$ 9.5 Hz, H-2').
16: m.p. 128-129°C (ethanol), $[\alpha]_D$ +10°; δ_H: 2.35 (1 H, ddd, $J_{1',2'eq}$ 2.5, $J_{2'eq,2'ax}$ 12.5, $J_{2'eq,3'}$ 4.5 Hz, H-2'eq), 1.63 (1 H, ddd, $J_{1',2'ax}$ 10, $J_{2'ax,3'}$ 9.5 Hz, H-2'ax).
17: m.p. 117°C (AcOEt-hexane), $[\alpha]_D$ +10°; δ_H: 4.42 (1 H, d, $J_{1',2'}$ 8 Hz, H-1').
18: m.p. 100°C (ethanol), $[\alpha]_D$ +7°; δ_H: 4.24 (1 H, dd, $J_{1',2'ax}$ 9.5 , $J_{1',2'eq}$ 2.0 Hz, H-1').
19: $[\alpha]_D$ +9°; δ_H: 5.33 (1 H, dd, $J_{1',2'}$ 8.0, $J_{2',3'}$ 10 Hz, H-2').
20: $[\alpha]_D$ -3°, δ_H: 4.75 (1 H, dd, $J_{1',2'eq}$ 2.0, $J_{1',2'ax}$ 10 Hz, H-1').
21: m.p. 150-151°C (ethanol), $[\alpha]_D$ +25°; δ_H (C_6D_6): 4.75 (1 H, d, $J_{1,2}$ 9.5 Hz, H-1), 4.55 (1 H, d, $J_{1',2'}$ 8.0 Hz, H-1').
22: m.p. 136-138°C (ethanol), $[\alpha]_D$ +6°, δ_H (C_6D_6): 4.63 (1 H, d, $J_{1,2}$ 9.5 Hz, H-1), 4.36 (1 H, dd, $J_{1',2'eq}$ 2.0, $J_{1',2'ax}$ 10 Hz, H-1').
13 T. Ogawa, K. Beppu and S. Nakabagashi, Carbohydr. Res., 93 C6-C9 (1981); H. Paulsen and M. Paal, Carbohydr. Res., 135, 53 (1984).
14 5 (84%); $[\alpha]_D$ +23°; δ_H: 5.62 (1 H, d, $J_{1,2}$ 8.5 Hz, H-1). It was prepared from known 3,4,6-tri-*O*-benzyl-1,2-*O*-(1-methoxyethylidene)-α-D-galactopyranose[15].
15 H.F. Vernay, E.S. Rachaman, R. Eby and C. Schuerch, Carbohydr. Res., 78, 267 (1980).
16 6: m.p. 112-113°C (ethanol), $[\alpha]_D$ +24°; δ_H: 5.66 (1 H, d, $J_{1,2}$ 8.5 Hz, H-1) was prepared from 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranosyl bromide[17] by conventional methods.
17 W. Schüep and E. Hardegger, Helv. Chim. Acta, 53, 1136 (1970).
18 J. Thiem and H. Karl, Chem. Ber., 113, 3039 (1980).
19 7: m.p. 109-110°C, $[\alpha]_D$ +14° was prepared from methyl 3,4-*O*-isopropylidene-β-D-galactopyranoside[20].
20 A. Stoffyn and P. Stoffyn, J. Org. Chem., 32, 4001 (1967).
21 8: m.p. 89-90°C (CH_2Cl_2-hexane), $[\alpha]_D$ -31° was prepared from phenyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside[22].
22 A. Lipták, I. Jodál, J. Harangi and P. Nánási, Acta Chim. Hung., 113, 415 (1983).
23 R. Eby and C. Schuerch, Carbohydr. Res., 34, 79 (1974); B. Bernet and A. Vasella, Helv. Chim. Acta, 62, 1990 (1979).
24 J.M. Küster and I. Dyong, Liebigs Ann. Chem., 2179 (1975).

(Received in France 13 February 1989)