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GLYCOSYLATIONS WITH *N*-FORMYLAMINO SUGARS: A NEW APPROACH TO 2'-DEOXY-β-DISACCHARIDES[1]

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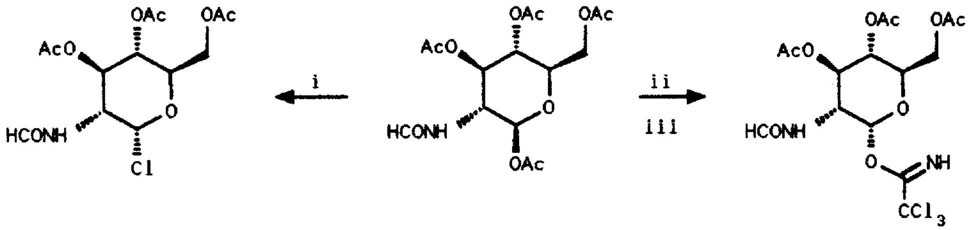
Abstract: Various derivatives of *N*-formyl glucosamine (β-acetate, α-chloride, α-trichloroacetimidate) are used as glycosyl donors. The resulting disaccharides are smoothly deaminated into the corresponding 2'-deoxy-β-disaccharides through intermediate isonitriles by radical reduction.

Barton <u>et al</u>.[2] reported in 1980 the radical deamination of 1,3,4,6-tetra-<u>O</u>-acetyl-2-deoxy-2-formamido-β-D-glucopyranose <u>1</u>[3] as an elegant entry to 1,3,4,6-tetra-<u>O</u>-acetyl-2-deoxy-β-D-glucopyranose. We thus decided to explore the β-glycosylating ability of <u>1</u> and derivatives as a nice adjunct to the Barton deamination, since it would open a novel route to 2'-deoxy-β-disaccharides, the importance of which has been stressed in the preceding letter of this issue.

Compound <u>1</u> was first converted[4] into either the crystalline α-chloride <u>2</u> or the α-trichloroacetimidate <u>3</u> as shown in Scheme I :



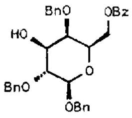
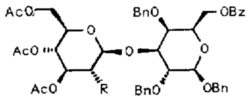
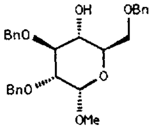
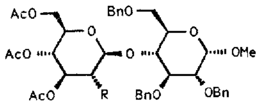
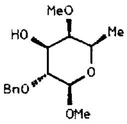
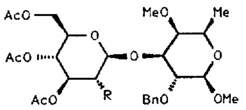
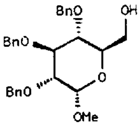
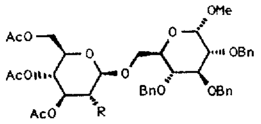
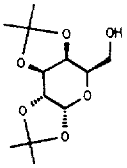
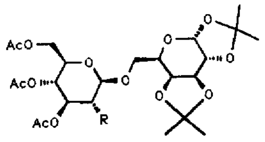
<u>2</u> <u>1</u> <u>3</u>

SCHEME I

Reagents: *i)* CH_3COCl-HCl, 25°C, 12 h (80%); *ii)* $C_6H_5CH_2NH_2$, THF, 25°C, 12 h (84%); *iii)* CCl_3CN, DBU, 4 Å MS, CH_2Cl_2, 0°C, 30 min (95%).

Depending on the structure of the glycosyl acceptor, the most appropriate glycosylation procedure was selected (either A, B or C) (Table I). The β-acetate <u>1</u> (method A) appeared as a good glycosyl donor in the presence of trimethylsilyltriflate with secondary alcohols <u>4</u> and <u>5</u>. The α-chloride <u>2</u> (method B) acted as a good donor in the presence of silver triflate with primary alcohols <u>7</u> and 1,2:3,4-di-<u>O</u>-isopropylidene-α-D-galactopyranose. In the case of alcohol <u>6</u>, α-trichloroacetimidate <u>3</u> (method C) appeared as a

TABLE 1

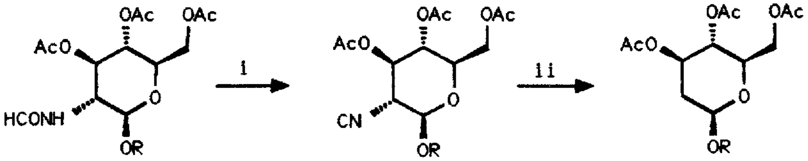
GLYCOSYL ACCEPTOR	DISACCHARIDE[13]	METHOD (Glycosylation Yield %)
 4[10]	 8 R = NHCHO 9 R = NC 10 R = H	A (94) B (27)
 5[12]	 11 R = NHCHO 12 R = NC 13 R = H	A (64) B (15)
 6[12]	 14 R = NHCHO 15 R = NC 16 R = H	A (29) B (26) C (64)
 7[12]	 17 R = NHCHO 18 R = NC 19 R = H	A (64) B (97)
	 20 R = NHCHO 21 R = NC 22 R = H	A (no condensation) B (83)

Method A: ROH (1 equiv.), *β-acetate* 1 (2 equiv.), TMSOTf (3 equiv.), 4 Å MS, CH_2Cl_2, room temperature until there was no more evolution as indicated by t.l.c. (6-48 h).

Method B: ROH (1 equiv.), *α-chloride* 2 (1.7 equiv.), AgOTf (2 equiv.), 4 Å MS, CH_2Cl_2 room temperature until there was no more evolution (24-48 h).

Method C: ROH (1 equiv.), *α-trichloroacetimidate* 3 (1.2 equiv.), TMSOTf (1.2 equiv.), 4 Å MS, CH_2Cl_2, room temperature, 24 h.

reasonable glycosyl donor, although the yield was rather modest[6]. The β-stereocontrol was attributed to the participating property of the *N*-formyl group[8]. The 2'-deoxy-2'-formamido disaccharides were deaminated according to Scheme II with total yields in the range of 65-89% (see Table I).



SCHEME II

Reagents: *i)* $POCl_3$, NEt_3, CH_2Cl_2[9]; *ii)* Bu_3SnH, toluene, reflux.[2]

We believe that this new approach and the one outlined in the preceding letter offer a rather general solution to the important problem of the practical synthesis of 2'-deoxy-β-disaccharides.

References and notes

1 Part of this work was presented at the 4th European Carbohydrate Symposium, Darmstadt (Germany), A-122, 1987.

2 D.H.R. Barton, G. Bringmann, G. Lamotte, W.B. Motherwell, R.S.H. Motherwell and A.E.A. Porter, J. Chem. Soc., Perkin Trans. I, 2657 (1980).

3 C.G. Greig, D.H. Leaback and P.G. Walker, J. Chem. Soc., 879 (1961).

4 All new compounds gave satisfactory microanalytical and spectral data. Values of $[\alpha]_D$ and δ_H or δ_C were measured for $CHCl_3$ and $CDCl_3$ solutions at 20° and 25°C, respectively, unless otherwise stated.
2 (80%): m.p. 105-107°C (CH_2Cl_2-benzene), $[\alpha]_D$ +106°; δ_H: 6.20 and 6.15 (1 H, 2 d, $J_{1,2}$ 3.5 Hz, H-1 of a 1:9 *cis-trans* mixture)[5].
3 (80%): $[\alpha]_D$ +87°; δ_H: 6.46 (1 H, d, $J_{1,2}$ 3.5 Hz, H-1).

5 ^1H-N.m.r. spectra of *N*-formyl derivatives of glucosamine reveal that these compounds exist in both the *cis* and *trans* configurations about the central C-N bond; L.A. Laplanche and M.T. Rogers, J. Am. Chem. Soc., 86, 337 (1964).

6 Compounds 6 and 14 are partially anomerized at their reducing end under the acidic conditions of the glycosylations. It was therefore found more advantageous to glycosylate 6 (or any acid sensitive alcohol) with the 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl trichloroacetimidate[7] in the presence of TMSOTf (-70°C, a few min, 93%). The following sequential treatment: *i)* NaOMe; *ii)* N_2H_4, ethanol, reflux; *iii)* *p*-nitrophenyl formate, dioxane-water; *iv)* acetic anhydride-pyridine , gave 14 (85%).

7 G. Grundler and R.R. Schmidt, Carbohydr. Res., 135, 203 (1985).

8 An oxazoline was isolated in 86% yield when the chloride 2 was treated with silver triflate, with the reaction mixture being neutralized with triethylamine after 4 h at 20°C; $[\alpha]_D$ +23°; δ_H: 7.20 (1 H, d, $J_{2,N=CH}$ 2.5 Hz, N=CH), 6.08 (1 H, d, $J_{1,2}$ 7.5 Hz, H-1), 5.36 (1 H, dd, $J_{2,3}$ 2.8, $J_{3,4}$ 2.2 Hz, H-3), 4.96 (1 H, ddd, $J_{2,4}$ 1.1, $J_{4,5}$ 9.0 Hz, H-4).

9 U. Schöllkopf, R. Schröder and D. Stafforst, Liebigs Ann. Chem., 44 (1974); G.D. Hartman and L.M. Weinstock, Org. Synth., 59, 182 (1979).

10 4: m.p. 77°C (diisopropyl ether), $[\alpha]_D$ -38°, was obtained by selective benzoylation of benzyl 2,4-di-*O*-benzyl-β-D-galactopyranoside[11] with benzoyl cyanide.

11 S. David, C.A. Johnson and A. Veyrières, Carbohydr. Res., 28, 121 (1973).

12 See the preceding letter of this issue for the preparation of 5, 6 and 7.

13 Selected physical data for disaccharides:

8: m.p. 157-159°C (ethanol), $[\alpha]_D$ -55°; δ_C: 102.06, 101.97 and 101.93 (C-1 and C-1' of a *cis-trans* mixture).

9: $[\alpha]_D$-25°;δ_H (C_6D_6): 4.44 (1 H, d, $J_{1',2'}$ 7.5 Hz, H-1').

10: $[\alpha]_D$ -49°, δ_H (C_6D_6): 4.66 (1 H, dd, $J_{1',2'eq}$ 2.0, $J_{1',2'ax}$ 9.5 Hz, H-1').

11: m.p. 160-162°C (methanol), $[\alpha]_D$ -28°; δ_C: 100.23 and 100.13 (C-1').

12: $[\alpha]_D$ +14°; δ_H (C_6D_6): 4.24 (1 H, d, $J_{1',2'}$ 8.0 Hz, H-1').

13: $[\alpha]_D$ +6°; δ_H (C_6D_6): 4.70 (1 H, dd, $J_{1',2'eq}$ 2.0, $J_{1',2'ax}$ 10.0 Hz, H-1').

14: m.p. 202-208°C (hexane-acetone), $[\alpha]_D$ +2°; δ_C: 109.39 and 104.44 (C-1').

15: $[\alpha]_D$ +34°; δ_H (C_6D_6): 4.80 (1 H, d, $J_{1',2'}$ 8.0 Hz, H-1').

16: $[\alpha]_D$ + 0.2°; δ_H (C_6D_6): 4.81 (1 H, dd, $J_{1',2'eq}$ 2.0, $J_{1',2'ax}$ 9.5 Hz, H-1').

17: m.p. 185-186°C (ethanol), $[\alpha]_D$ +12°; δ_C: 101.20 and 100.16 (C-1').

18: $[\alpha]_D$ +34°; δ_H: 4.46 (1 H, d, $J_{1',2'}$ 8.0 Hz, H-1').

19: $[\alpha]_D$ +20°; δ_H (C_6D_6): 4.07 (1 H, dd, $J_{1',2'eq}$ 2.5, $J_{1',2'ax}$ 9.5 Hz, H-1').

20: m.p. 143-144°C (hexane-acetone), $[\alpha]_D$ -67°; δ_H: 4.80 (1 H, d, $J_{1',2'}$ 8.5 Hz, H-1'); δ_C: 101.92 and 101.01 (C-1').

21: $[\alpha]_D$ -28°: δ_H: 4.87 (1 H, d, $J_{1',2'}$ 8.0 Hz, H-1').

22: m.p. 115°C (diisopropyl ether), $[\alpha]_D$ -68°; δ_H: 4.30 (1 H, dd, $J_{1',2'eq}$ 2.0, $J_{1',2'ax}$ 9.5 Hz, H-1').

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