Stereoselective Synthesis of Mixed Acetal Glycosides by Reaction of Tri-*O*-acetyl-*N*-(2,4-dinitrophenyl)-α-D-glucosaminyl Bromide with Alcohol in Acetone[1]

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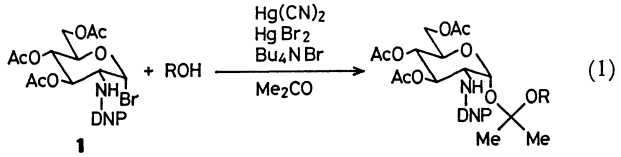
Synopsis. Some mixed acetal glycosides were stereoselectively synthesized by the reaction of 3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-α-D-glucopyranosyl bromide with alcohols in acetone containing $Hg(CN)_2$, $HgBr_2$, and tetrabutylammonium bromide at room temperature. When *t*-butyl alcohol was used, a novel enol glycoside of acetone was formed.

3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-α-D-glucopyranosyl bromide (**1**)[2] has been a useful reagent for synthesizing various α-D-glucosaminides.[3] This report presents our findings that a homogeneous reaction of **1** with methanol (MeOH) in acetone (Me_2CO) in the presence of $Hg(CN)_2$, $HgBr_2$, and tetrabutylammonium bromide (*n*-Bu_4NBr) at room temperature gave a novel acetal glycoside (**2**) (Eq. 1) in a 54% yield (Table 1, Run 2).[4] The reaction was highly stereoselective and gave no methyl glycosides (**3a** and **3b**). The use of solvents such as 1,2-dichloroethane (Run 9) and nitromethane (Run 10) as well as an excess of MeOH (Run 11) caused the



(1)

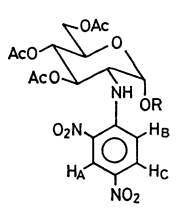
1

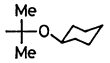
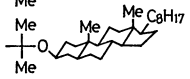
DNP = 2,4-dinitrophenyl

Table 1. Results of experiments using methanol[a]

Run	$Hg(CN)_2$ (equiv.)	$HgBr_2$ (equiv.)	*n*-Bu_4NBr (equiv.)	Yield/%[b] **2**	Yield/%[b] **3a**+**3b**
1	0.5	0.5	0.67	31	0
2	0.5	0.5	1.0	54	0
3	0.5	0.5	1.5	32	13
4	0.5	0.5	2.0	16	32
5	0.5	0.5	—	0	8
6	—	—	1.0	0	35
7	1.0	—	1.0	69	18
8	—	1.0	1.0	0	20
9[c]	0.5	0.5	1.0	35[f]	21
10[d]	0.5	0.5	1.0	60[f]	8
11[e]	0.5	0.5	1.0	53	19

a) Reactions were conducted in 0.1 mmol scale for 6 h at room temperature. b) Yields were determined by measuring ^1H NMR (60 MHz) of product mixtures (see Experimental). c) Me_2CO (66 μl, 9.0 equiv.) and $(CH_2Cl)_2$ (0.46 ml) were used. d) Me_2CO (66 μl, 9.0 equiv.) and $MeNO_2$ (0.46 ml) was used. e) Excess MeOH (12 μl, 3.0 equiv.) was used. f) A very small peak of the β-anomer of **2** was observed at δ 3.01.



Compound	R
2	
3a	-Me
4	
5	
6	
7	-H

formation of **3a** and **3b**. The use of the ternary mixture was essential for the acetalization without forming **3a** and **3b** (Runs 5—8); the optimal proportion of $Hg(CN)_2$, $HgBr_2$, and *n*-Bu_4NBr to **1** found is 0.5:0.5:1.0 (Runs 1—4).

Incidentally, 1-methoxy-1-methylethyl group, known as a labile protecting group of hydroxyl group,[5] was readily removed from **2** by a mild acid hydrolysis without the removal of the acetyl groups and survived through the *O*-deacetylation and the *N*-dedinitrophenylation in basic media.

2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl bromide does not undergo such acetalization reaction. For **1**, Me_2CO is the sole ketone which gives the acetal glycoside in an acceptable yield, aldehydes such as propional are also unsuitable. Cyclohexanol and 5α-cholestan-3β-ol gave the respective acetal glycosides (**4** and **5**). However, *t*-butyl alcohol did not afford such a type of glycoside but isopropenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-α-D-glucopyranoside (**6**), a novel enol glycoside,[6] was formed.

Experimental

The instruments used were identical with those described earlier.[7] Solid compounds, **1**,[2] $Hg(CN)_2$ (Wako), $HgBr_2$ (Wako), *n*-Bu_4NBr (Tokyo Kasei), and 5α-cholestan-3β-ol (Tokyo Kasei), were stored *in vacuo* over P_2O_5 before use. The physical and analytical data for the acetals are in Table 2.

*1-Methoxyl-1-methylethyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-α-D-glucopyranoside (2).* MeOH (40 μl, 1.0 mmol) and Me_2CO (5.3 ml) were successively added to a mixture of **1** (534 mg, 1.0 mmol), $Hg(CN)_2$ (126 mg, 1.0 mmol), $HgBr_2$ (180 mg, 1.0 mmol), and *n*-Bu_4NBr (322 mg, 1.0 mmol). After stirring for 24 h at room temperature and adding water (1.0 ml), the mixture was evaporated at 30 °C under diminished pressure and chromatographed on silica gel (Kanto Kagaku) using a mixture of benzene and butanone (10:1). The faster-moving band afforded **2** (310.5 mg, 57%); δ_H ($CDCl_3$, Me_4Si): 1.50 (s, 6H, CMe), 1.80 (s, 3H, OAc),

Table 2. Yields[a] and physical data of acetals

Compd	Yield %	Mp(recrystallized from[b]) θ_m/°C		$[\alpha]_D^{20}$/° (c, Me_2CO)	Mol formula	Found(Calcd)(%) C	H	N
2	54	174—176	(C/H, needles)	+12(1.0)	$C_{22}H_{29}N_3O_{13}$	48.38 (48.62)	5.29 (5.38)	7.89 (7.73)
4	69	173—175	(I, needles)	+9(0.5)	$C_{27}H_{37}N_3O_{13}$	52.88 (53.02)	5.81 (6.10)	6.71 (6.87)
5	64	228—230(decomp)	(E, needles)	+71(0.6)	$C_{40}H_{73}N_3O_{13}$	63.93 (64.05)	8.10 (8.17)	4.58 (4.67)

a) Reaction time was 6 h. b) C: Chloroform, E: ethyl acetate, H: hexane, I: diisopropyl ether.

2.06 (s, 3H, OAc), 2.10 (s, 3H, OAc), 3.19 (s, 3H, OMe), 7.07 (d, 1H, J_{BC}=10 Hz, H_B), 8.27 (q, 1H, H_C), 8.72 (d, 1H, J=10 Hz, NH), 9.10 (d, 1H, J_{AB}=3.5 Hz, H_A); δ_C ($CDCl_3$, Me_4Si)[8] 20.6 (3C, OAc), 24.6, 26.3, 50.0 (OMe), 55.3 (C-2), 62.1 (C-6), 67.9, 68.4, 72.9, 90.1 (C-1), 103.3 (C-α), 114.5, 124.3, 130.0, 131.0, 136.7, 147.5, 169.6, 169.9, 170.7. The slower-moving band gave 3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-α-D-glucopyranose (**7**) (170.5 mg, 38%), which was identified with the sample prepared by the authentic route.[2]

Heating **2** (52.6 mg, 0.097 mmol) in aq acetic acid (80%, 0.5 ml) at 70 °C for 40 min furnished **7** (42.5 mg, 93%).

*1-Methoxy-1-methylethyl 2-Deoxy-2-(2,4-dinitroanilino)-α-D-glucopyranoside (**8**).* The treatment of **2** (200 mg, 0.37 mmol) with ammoniacal methanol (38 g, 21%) at room temperature overnight gave **8** (*ca.* 150 mg, quant.); mp 160—162 °C, $[\alpha]_D^{20}$ +4.5° (*c* 1.0, Me_2CO); δ_H (($CD_3)_2CO$, Me_4Si) 1.43 (s, 3H, CMe), 1.48 (s, 3H, CMe), 3.16 (s, 3H, OMe), 5.40 (d, 1H, $J_{1,2}$=3.5 Hz, H-1), 7.53 (d, 1H, J_{BC}=10 Hz, H_B), 8.25 (q, 1H, H_C), 8.97 (d, 1H, J_{AB}=2.5 Hz); δ_C (($CD_3)_2CO$, Me_4Si) 24.9, 26.7, 49.8 (OMe), 57.8 (C-2), 62.4 (C-6), 71.5, 73.4, 75.1, 91.2 (C-1), 102.8 (C-α), 117.2, 124.1, 130.2, 130.9, 136.5, 149.7. Found: C, 45.79; H, 5.44; N, 10.04%. Calcd for $C_{16}H_{23}N_3O_9$: C, 46.04; H, 5.55; N, 10.07%.

*1-Methoxy-1-methylethyl 2-Amino-2-deoxy-α-D-glucopyranoside (**9**).* The treatment of **8** (91.8 mg, 0.22 mmol) with Dowex 1×2 (1 ml) in aq Me_2CO (67%, 5 ml) for 6 h at room temperature afforded **9** (41.1 g, 74%); mp 189—191 °C (decomp), $[\alpha]_D^{20}$ +139° (*c* 0.3, H_2O); δ_H (D_2O, Me_4Si (ext.)) 1.90 (s, 6H, CMe), 3.16 (dd, 1H, J=3.9 and 9.6 Hz, H-2), 3.76 (s, 3H, OMe) 5.64 (d, 1H, J=3.9 Hz H-1); δ_C (D_2O, Me_4Si (ext.)) 25.2, 26.2, 50.7 (OMe), 56.5 (C-2), 62.0 (C-6), 71.2 (C-4), 73.6 (C-5), 75.2 (C-3), 93.8 (C-1), 103.9 (C-α). Found: C, 47.65; H, 8.52; N, 5.55%. Calcd for $C_{10}H_{21}NO_6$: C, 47.80; H, 8.42; N, 5.57%.

Procedure for the Acetalization to Obtain the Data for Table 1. A round-bottomed flask containing weighed solid compounds (**1** and, optionally, $Hg(CN)_2$, $HgBr_2$ and *n*-Bu_4NBr) was kept *in vacuo* over P_2O_5 for 30 min. Anhydrous solvent (when necessary), Me_2CO, and MeOH were successively injected into this vessel, stoppered with a rubber-cap. The reaction was stirred and quenched by adding water (1 drop). After evaporation at 30 °C, the mixture was chromatographed as above. Fractions containing **2**, **3a**, and **3b** were combined to give a glass whose ^1H NMR spectrum usually showed three singlets of methoxyl groups of **2**, **3a**, and **3b** at δ 3.20, 3.55, and 3.50 in $CDCl_3$ with Me_4Si (Table 1).

Attempted Acetalization Using t-*Butyl Alcohol.* Me_2CO (1.0 ml) was injected into a rubber-stoppered flask containing *t*-BuOH (15.2 mg, 0.2 mmol), **1** (106.8 mg, 0.2 mmol), $Hg(CN)_2$ (25.2 mg, 0.1 mmol), $HgBr_2$ (36.0 mg, 0.1 mmol), and *n*-Bu_4NBr (64.4 mg, 0.2 mmol). After having been stirred for 6 h at room temperature, the mixture was evaporated and chromatographed as above. The faster-moving major band gave isopropenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-α-D-glucopyranoside (**6**) (37.1 mg, 36%); mp 199—202 °C, $[\alpha]_D^{20}$ −8.6° (*c* 1.3, Me_2CO); δ_H ($CDCl_3$, Me_4Si) 1.77 (s, 3H, OAc), 1.90 (s, 3H, CMe), 1.97 (s, 3H, OAc), 2.03 (s, 3H, OAc), 7.10 (d, 1H, J_{BC}=9 Hz, H_B), 8.20 (q, 1H, H_C), 8.80 (d, 1H, J=12 Hz, NH), 9.07 (d, 1H, J_{AB}=3 Hz, H_A); δ_C ($CDCl_3$, Me_4Si) 20.2 (CMe), 20.6 (3C, Ac), 55.1 (C-2), 61.5 (C-6), 67.9, 68.3, 73.0, 88.7 (C-β), 94.7 (C-1), 114.4, 124.3, 130.0, 131.3, 136.9, 147.6, 157.1 (C-α) 169.7 (2C, Ac), 170.7 (Ac). Found: C, 48.94; H, 4.84; N, 8.41%. Calcd. for $C_{21}H_{25}N_3O_{12}$: C, 49.32; H, 4.93; H, 8.22%.

Compound **6** (45.7 mg, 0.09 mmol) was treated with dil. sodium methoxide in methanol (0.15%, 2 ml) at room temperature overnight. After NH_4Cl had been added, the mixture was evaporated and chromatographed to give propenyl 2-deoxy-2-(2,4-dinitroanilino)-α-D-glucopyranoside (**10**) (35 mg, 94%); mp 161—165 °C, $[\alpha]_D^{20}$ −1.0° (*c* 1.4, Me_2CO); δ_H (($CD_3)_2CO$, Me_4Si) 1.95 (s, 3H, CMe), 5.48 (d, 1H, $J_{1,2}$=3.5 Hz, H-1), 7.57 (d, 1H, J_{BC}=9 Hz, H_B), 8.23 (q, 1H, H_C), 8.95 (d, 1H, J_{AB}=3 Hz, H_A); δ_C (($CD_3)_2CO$, Me_4Si)[6] 20.4 (CMe), 58.1 (C-2), 62.0 (C-6), 71.0, 74.4, 75.6, 88.3 (C-β), 96.6 (C-1), 117.3, 124.4, 130.5, 131.5, 131.6, 137.2, 150.1, 158.4 (C-α). Found: N, 10.42%. Calcd for $C_{15}H_{19}N_3O_9$: N, 10.90%.

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8) Assignments were carried out by observing off-resonance decoupling spectra.