Carbohydrate Research, 184 (1988) 262–267
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

Note

Nucleophilic displacement reactions of some *N*-acetyl-*N*-*p*-chlorophenyl-β-D-ribopyranosylamine derivatives

ZYGFRYD SMIATACZ
Institute of Chemistry, University of Gdańsk, 80-952 Gdańsk (Poland)

AND ANTONINA MOCZULSKA
Department of Chemistry, The Pedagogical University, 76-200 Słupsk (Poland)

(Received March 10th, 1988; accepted for publication, May 21st, 1988)

Previous studies have been concerned with the nucleophilic displacement reactions of derivatives of *N*-acetyl-*N*-aryl-β-D-xylopyranosylamines[1]. We now report analogous investigations with some derivatives of *N*-acetyl-*N*-*p*-chlorophenyl-β-D-ribopyranosylamine. *N*-Acetyl-*N*-aryl-D-pentopyranosylamines have properties which resemble those of certain nucleosides[2] and may be considered as model compounds suitable for studying S_N2 reactions in *N*-glycosyl derivatives.

Reaction of *N*-acetyl-*N*-*p*-chlorophenyl-β-D-ribopyranosylamine (**1**) with 3 equiv. of benzoyl chloride in pyridine gave a mixture of five products which were isolated by chromatography and identified as the 2,3,4-tri- (**2**), 2,4-di- (**3**), 3,4-di- (**4**), 3- (**5**), and 4-benzoate (**6**). The structures of **3**–**6** were established on the basis of ^{1}H-n.m.r. data (Table I). That HO-2 in **4**–**6**, HO-3 in **3** and **6**, and HO-4 in **5** were unsubstituted was indicated by a large downfield shift (1.2–1.5 p.p.m.) of the signals for H-2, H-3, and H-4, respectively, on benzoylation or mesylation (→**2**, **7**, and **8**, respectively).

Treatment of the 3-mesylate **7** with sodium azide in *N*,*N*-dimethylformamide gave *N*-acetyl-3-azido-2,4-di-*O*-benzoyl-*N*-*p*-chlorophenyl-3-deoxy-β-D-xylopyranosylamine (**9**). The $^4C_1$-β-D-*xylo* structure of **9** was established on the basis of ^{1}H-n.m.r. data ($J_{1,2} \approx J_{2,3} \approx J_{3,4} \approx J_{4,5a} \approx 10$, $J_{4,5e}$ ~3 Hz; $\Delta\delta_{H\text{-}5e,5a}$ ~0.70, Table I). Hydrogenolysis of **9** over Pd/C and acetylation of the product gave 3-acetamido-*N*-acetyl-2,4-di-*O*-benzoyl-*N*-*p*-chlorophenyl-3-deoxy-β-D-xylopyranosylamine (**10**). Attempts to displace MsO-3 of **7** with sodium azide in acetonitrile failed.

Reaction of the 2-mesylate **8** with sodium azide in *N*,*N*-dimethylformamide at ~130° gave the D-*arabino* product **11**, whereas, with acetonitrile as solvent, the two D-*arabino* products **11** and **12** were obtained in the ratio ~1:1. Compound **11** had i.r. absorption for NH but not for amide C=O, and the n.m.r. spectrum indicated the presence of an OAc group (δ ~1.92, Table I). Acetylation of **11** gave

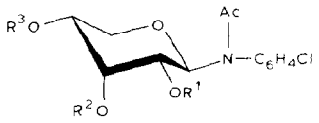
0008-6215/88/$ 03.50

TABLE I

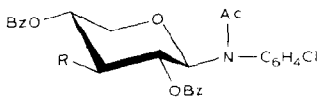
^{1}H-N.M.R. DATA[a] FOR COMPOUNDS **2–14**

Compound	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*e	*H-5*a	$\Delta\delta_{H\text{-}5e,H\text{-}5a}$	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5e}$	$J_{4,5a}$	*NAc*	*OAc*	*OMs*
2	6.62d	4.65dd	6.12dd	5.22m	4.20dd	4.15dd	0.05	10	3	3	2.5	9	1.72		
3	6.52d	4.45dd	4.62dd	4.98m	4.10	3.98	0.12	10	2.5	2.5	2.5	10	1.70		
4	6.20d	3.34dd	5.88dd	5.02m	4.05	3.95	0.10	9	3	3	3	9	1.75		
5	6.02d	3.12dd	5.52dd	3.75	—	3.22		9	3	3	3	10	1.62		
6	6.08d	3.10dd	4.32dd	4.82m	3.96	3.80	0.08	9	3	3	3	9	1.68		
7	6.60d	4.65dd	5.65dd	5.23m	4.25–4.07			10	3	3	3	10	1.80		2.92
8	6.45d	4.57dd	6.18dd	5.12m	4.17–4.05			10	3	3	3	10	1.80		2.95
9	6.35d	4.85dd	4.05dd	5.15m	4.30dd	3.60dd	0.70	10	10	10	3	10	1.75		
10	6.25d	4.75dd	4.50dd	5.15m	4.35	3.75dd	0.60	10	10	10	3	10	1.62 1.80		
11	5.75	—	—	—	—	3.75m								1.92	
12	6.12d	5.60dd	5.75m	5.52m	4.35dd	4.12dd	0.22	2.5	2.5		3	10	1.77		
13	6.25d	5.37dd	5.72–5.57m		4.25dd	3.95dd	0.70	10	10		3	3	1.85	2.00	
14	6.37d	6.00dd	5.50–5.32m		4.22dd	4.12dd	0.10	2.5	2.5				1.82		3.07

[a]Chemical shifts (δ scale) with coupling constants (Hz, ±0.5 Hz) determined by first-order analysis.



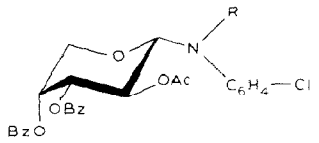
1 $R^1 = R^2 = R^3 = H$
2 $R^1 = R^2 = R^3 = Bz$
3 $R^1 = R^3 = Bz, R^2 = H$
4 $R^1 = H, R^2 = R^3 = Bz$
5 $R^1 = R^3 = H, R^2 = Bz$
6 $R^1 = R^2 = H, R^3 = Bz$
7 $R^1 = R^3 = Bz, R^2 = Ms$
8 $R^1 = Ms, R^2 = R^3 = Bz$



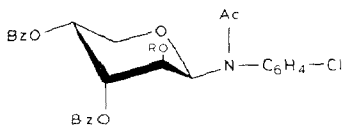
9 R = N_3
10 R = NHAc

13, which had an i.r. band at 1685 cm^{-1} (amide CO), and the n.m.r. data [$J_{1,2} \approx J_{2,3} \approx 10$, $J_{4,5e} \approx J_{4,5a} \approx 3$ Hz; $\delta \sim 1.85$ (NAc) and ~2.0 (OAc)] indicated it to be *N*-acetyl-2-*O*-acetyl-3,4-di-*O*-benzoyl-*N*-*p*-chlorophenyl-α-D-arabinopyranosylamine with the $^1C_4$ conformation.

The identification of **12** as *N*-acetyl-3,4-di-*O*-benzoyl-*N*-*p*-chlorophenyl-β-D-arabinopyranosylamine with the $^4C_1$ conformation was also based on the i.r. [bands at 3400 (OH) and 1660 cm^{-1} (amide CO)] and ^{1}H-n.m.r. data [$J_{1,2} \approx J_{2,3} \approx J_{4,5e} \approx 3$, $J_{4,5a} \sim 10$ Hz; $\delta \sim 1.77$ (NAc)]. That HO-2 in **12** was unsubstituted was indicated by comparison of the n.m.r. data with those of **14**, there being a downfield shift (~0.40 p.p.m.) of the signal for H-2 on mesylation (Table I).



11 R = H
13 R = Ac

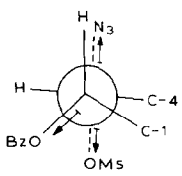


12 R = H
14 R = Ms

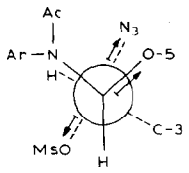
Thus, **8** undergoes solvolysis of MsO-2 with participation of the *N*-acetyl group on treatment with sodium azide in *N*,*N*-dimethylformamide or acetonitrile. The displacement of MsO-2 by azide did not occur, probably due to unfavourable steric and polar interactions in the transition state[3-7], although it has been effected in the β-D-*manno* series[7,8].

No reaction occurred on treatment of **14** with sodium azide in *N*,*N*-dimethylformamide at ~130°, probably because MsO-2 and N-Ac are *cis*.

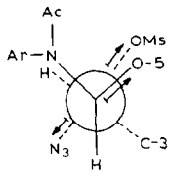
The differences in the reactivity of MsO-2 and MsO-3 in the derivatives of *N*-acetyl-*N*-aryl-β-D-ribo- (**7** and **8**) and β-D-arabino-pyranosylamine (**14**) can be elucidated in terms of steric and polar interaction in the transition states[5,7,9,10] as illustrated by the Newman projections along the C-2–C-3 (**15** for **7**) and C-1–C-2 (**16** and **17** for **8** and **14**, respectively) bonds.



15



16



17

EXPERIMENTAL

Melting points are uncorrected. Optical rotations were determined (Hilger–Watt instrument) for solutions in chloroform (c ~0.5). T.l.c. was performed on Silica Gel G with *A*, carbon tetrachloride–acetone (3:1); *B* (6:1); *C*, benzene–acetone (6:1); or *D*, di-isopropyl ether–cyclohexane (2:1). Column chromatography was performed on Kieselgel (<0.08 mm). ^{1}H-N.m.r. spectra ($CDCl_3$, internal Me_4Si) were recorded with a Tesla BS 487 C (80 MHz) spectrometer. I.r. spectra were recorded for Nujol mulls with a Perkin–Elmer 257 spectrophotometer. F.d.-mass spectra were recorded on a MAT 711 mass spectrophotometer.

N-Acetyl-*N*-*p*-chlorophenyl-β-D-ribopyranosylamine (**1**), m.p. 158–161°, $[\alpha]_D^{20}$ +34° (lit.[11] m.p. 158–160°, $[\alpha]_D^{20}$ +33°), was prepared according to the literature procedure[11].

Selective benzoylation of N-*acetyl*-N-p-*chlororphenyl*-β-D-*ribopyranosylamine*[11] (**1**). — To a solution of **1** (0.06 mol) in dry pyridine (70 mL) at −10° was added benzoyl chloride (0.18 mol) dropwise during ~30 min. The mixture was kept for 1 h at ~0° and for ~20 h at +20°. T.l.c. (solvent *A*) then indicated complete conversion of **1** into five products. Chloroform (200 mL) was added, the mixture was poured into ice and water, and the chloroform layer was washed with aqueous 2–3% sulfuric acid and aqueous 5% sodium hydrogencarbonate, dried (Na_2SO_4), and concentrated. Column chromatography (solvent *D*) of the syrupy residue gave *N*-acetyl-2,3,4-tri-*O*-benzoyl-*N*-*p*-chlorophenyl-β-D-ribopyranosylamine (**2**, 16%), m.p. 176–177°, $[\alpha]_D^{20}$ −42°, R_F 0.8 (solvent *D*); lit.[11] m.p. 176–178°, $[\alpha]_D^{20}$ −45°.

Eluted second was *N*-acetyl-2,4-di-*O*-benzoyl-*N*-*p*-chlorophenyl-β-D-ribopyranosylamine (**3**, 28%), m.p. 183–185°, $[\alpha]_D^{21}$ −27°, R_F 0.53; lit.[11] m.p. 182–185°, $[\alpha]_D^{20}$ −28° (acetone).

Eluted third was *N*-acetyl-3,4-di-*O*-benzoyl-*N*-*p*-chlorophenyl-β-D-ribopyranosylamine (**4**, 15%), m.p. 202–203°, $[\alpha]_D^{20}$ −12°, R_F 0.34; ν_{max} 3360 (OH), 1730 (ester CO), and 1670 cm^{-1} (amide CO).

Anal. Calc. for $C_{27}H_{24}ClNO_7$: C, 63.68; H, 4.70; N, 2.75. Found: C, 63.73; H, 4.78; N, 2.80.

Eluted fourth was *N*-acetyl-3-*O*-benzoyl-*N*-*p*-chlorophenyl-β-D-ribopyranosylamine (**5**, 8%), m.p. 118–120°, $[\alpha]_D^{20}$ −16°, R_F 0.30; ν_{max} 3450, 3480 (OH), 1735 (ester CO), and 1665 cm^{-1} (amide CO).

Anal. Calc. for $C_{20}H_{20}ClNO_6$: C, 59.18; H, 4.93; N, 3.45. Found: C, 59.25; H, 4.96; N, 3.61.

Eluted fifth was *N*-acetyl-4-*O*-benzoyl-*N*-*p*-chlorophenyl-β-D-ribopyranosylamine (**6**, 17%), m.p. 119–122°, $[\alpha]_D^{20}$ +31°, R_F 0.25; lit.[11] m.p. 121–124°, $[\alpha]_D^{20}$ +29°.

N-*Acetyl-2,4-di-O-benzoyl*-N-p-*chlorophenyl-3-O-methanesulphonyl* (**7**) *and* N-*acetyl-3,4-di-O-benzoyl*-N-p-*chlorophenyl-2-O-methanesulphonyl-β-D-ribopyranosylamine* (**8**). — Conventional treatment of **3** (1 mmol) with pyridine (7 mL) and mesyl chloride (6 mmol) at 0° afforded **7** (62%), m.p. 162–167° (from methanol), $[\alpha]_D^{20}$ +9°, R_F 0.74 (solvent *A*) and 0.66 (solvent *C*); ν_{max} 1725 (ester CO), 1680 (amide CO), and 1190 cm^{-1} (OMs).

Anal. Calc. for $C_{28}H_{26}ClNO_9S$: C, 57.19; H, 4.42; N, 2.38. Found: C, 57.25; H, 4.48; N, 2.46.

Likewise, **4** gave **8** (75%), m.p. 156–158°, $[\alpha]_D^{20}$ +36°, R_F 0.82 (solvent *A*) and 0.70 (solvent *B*); ν_{max} 1720 (ester CO), 1675 (amide CO), and 1180 cm^{-1} (OMs).

Anal. Found: C, 57.18; H, 4.50; N, 2.48.

N-*Acetyl-3-azido-2,4-di-O-benzoyl*-N-p-*chlorophenyl-3-deoxy-β-D-xylopyranosylamine* (**9**). — A mixture of **7** (0.5 mmol) and sodium azide (2 mmol) in *N,N*-dimethylformamide (5 mL) was heated for 17 h at ~130°. T.l.c. (solvent *A*) then indicated reaction to be complete. The mixture was treated with acetone, filtered, and concentrated to dryness, and a solution of the residue in chloroform (50 mL) was washed with water (3 × 50 mL), dried ($MgSO_4$), and concentrated. Column chromatography of the residue (solvent *A*) gave **9**, as a syrup (~70%), $[\alpha]_D^{20}$ −27°, R_F 0.86 (solvent *A*); ν_{max} 2100 (N_3), 1740 (ester CO), and 1690 cm^{-1} (amide CO). Mass spectrum (f.d.): *m/z* 534 (M^+).

Anal. Calc. for $C_{27}H_{23}ClN_4O_6$: C, 60.61; H, 4.30; N, 10.47. Found: C, 60.38; H, 4.40; N, 10.35.

3-Acetamido-N-*acetyl-2,4-di-O-benzoyl*-N-p-*chlorophenyl-3-deoxy-β-D-xylopyranosylamine* (**10**). — A solution of **9** (0.35 mmol) in methanol (15 mL) was stirred under hydrogen (1 atm.) in the presence of 5% Pd/C (200 mg) for 30 h at ~20°. The catalyst was then removed, the filtrate was concentrated, and the residue was treated with pyridine–acetic anhydride to afford **10** as a syrup (~50%), $[\alpha]_D^{20}$ +10°, R_F 0.77 (solvent *A*); ν_{max} 3240 (NH), 1730 (ester CO), and 1680 cm^{-1} (amide CO). Mass spectrum (f.d.): *m/z* 550 (M^+).

Anal. Calc. for $C_{29}H_{27}ClN_2O_7$: C, 63.22; H, 4.90; N, 5.09. Found: C, 63.35; H, 4.97; N, 5.15.

Solvolyses of **8**. — (*a*) A mixture of **8** (1 mmol), sodium azide (4 mmol), and *N,N*-dimethylformamide (10 mL) was stirred for 4 h at ~130°. T.l.c. (solvent *B*) then indicated reaction to be complete. The mixture was treated with acetone, filtered, diluted with chloroform (50 mL), washed with water (3 × 50 mL), dried ($MgSO_4$), and concentrated to dryness. Column chromatography of the residue (solvent *B*) gave 2-*O*-acetyl-3,4-di-*O*-benzoyl-*N*-*p*-chlorophenyl-D-arabinopyranosylamine (**11**, 90%) as a syrup, $[\alpha]_D^{20}$ −202°, R_F 0.86 (solvent *A*) and 0.84 (solvent *B*); ν_{max} 3400 (NH) and 1735 cm^{-1} (ester CO).

Anal. Calc. for $C_{27}H_{24}ClNO_7$: C, 63.59; H, 4.71; N, 2.75. Found: C, 63.60; H, 4.76; N, 2.80.

(*b*) A mixture of **8** (1 mmol), sodium azide (4 mmol), and acetonitrile (20 mL) was stirred for 12 h at ~80°. T.l.c. (solvent *B*) then indicated reaction to be complete. The mixture was processed as in (*a*). Column chromatography (solvent *B*) gave, first, **11** (40%).

Eluted second was *N*-acetyl-3,4-di-*O*-benzoyl-*N*-*p*-chlorophenyl-β-D-arabinopyranosylamine (**12**, 45%), m.p. 152–155°, $[\alpha]_D^{20}$ +44°, R_F 0.79 (solvent *A*) and 0.63 (solvent *B*); ν_{max} 3400 (OH), 1735 (ester CO), and 1660 cm^{-1} (amide CO).

Anal. Calc. for $C_{27}H_{24}ClNO_7$: C, 63.59; H, 4.71; N, 2.75. Found: C, 63.65; H, 4.80; N, 2.77.

Treatment of **11** (0.5 mmol) with acetic anhydride (9 mL) and zinc chloride (0.05 g) afforded, after column chromatography (solvent *B*), *N*-acetyl-2-*O*-acetyl-3,4-di-*O*-benzoyl-*N*-*p*-chlorophenyl-α-D-arabinopyranosylamine (**13**, 35%), m.p. 151–153°, $[\alpha]_D^{20}$ −162°, R_F 0.74 (solvent *A*) and 0.64 (solvent *B*); ν_{max} 1735 and 1765 (ester CO), and 1685 cm^{-1} (amide CO). Mass spectrum (f.d.): *m/z* 551 (M^+).

Anal. Calc. for $C_{29}H_{26}ClNO_8$: C, 63.10; H, 4.71; N, 2.54. Found: C, 63.18; H, 4.70; N, 2.60.

Conventional treatment of **12** (0.3 mmol) with methanesulphonyl chloride (1.5 mmol) in pyridine gave, after column chromatography (solvent *A*), *N*-acetyl-3,4-di-*O*-benzoyl-*N*-*p*-chlorophenyl-2-*O*-methanesulphonyl-β-D-arabinopyranosylamine (**14**) as a syrup (66%), $[\alpha]_D^{20}$ +46°, R_F 0.85 (solvent *A*); ν_{max} 1735 (ester CO), 1675 (amide CO), and 1185 cm^{-1} (OMs).

Anal. Calc. for $C_{28}H_{26}ClNO_9S$: C, 57.19; H, 4.42; N, 2.38. Found: C, 57.23; H, 4.48; N, 2.40.

A solution of **7** (0.5 mmol) and sodium azide (2 mmol) in acetonitrile (5 mL) was heated for 12 h at 80°. T.l.c. (solvents *A* and *B*) then indicated that no reaction had occurred.

A solution of **14** (0.3 mmol) and sodium azide (2 mmol) in *N*,*N*-dimethylformamide (5 mL) was stirred for 70 h at ~130°. T.l.c. (solvents *A* and *B*) then indicated that no reaction had occurred.

REFERENCES

1 Z. Smiatacz and A. Moczulska, *Carbohydr. Res.*, 135 (1985) 219–229.
2 K. A. Watanabe, D. H. Hollenberg, and J. J. Fox, *J. Carbohydr. Nucleosides Nucleotides*, 1 (1974) 1–37.
3 L. Hough and A. C. Richardson, in S. Coffey (Ed.), *Rodd's Chemistry of Carbon Compounds*, 2nd edn., Vol. 1F, Elsevier, Amsterdam, 1967, pp. 223–238.
4 Y. Ali and A. C. Richardson, *J. Chem. Soc., C*, (1968) 1764–1769.
5 A. C. Richardson, *Carbohydr. Res.*, 10 (1968) 395–402.
6 D. H. Ball and F. W. Parrish, *Adv. Carbohydr. Chem. Biochem.*, 24 (1969) 159–164.
7 M. Miljković, M. Gligorijević, and D. Glišin, *J. Org. Chem.*, 39 (1974) 3223–3226.
8 A. Dessinges, A. Olesker, G. Lukacs, and T. T. Thang, *Carbohydr. Res.*, 126 (1984) c6–c8.
9 E. L. Eliel and R. G. Haber, *J. Am. Chem. Soc.*, 81 (1959) 1249–1254; E. L. Eliel and R. S. Ro, *ibid.*, 79 (1957) 5995–6000.
10 C. L. Stevens, K. G. Taylor, and J. A. Valicenti, *J. Am. Chem. Soc.*, 87 (1965) 4579–4584.
11 Z. Smiatacz and E. Paszkiewicz, *Rocz. Chem.*, 49 (1975) 909–917.