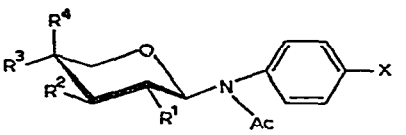
Carbohydrate Research, 39 (1975) 344–350

Note

Methyl ethers of some *N*-acetyl-*N*-arylpentopyranosylamines*

ZYGFRYD SMIATACZ
Institute of Chemistry, University of Gdansk, 80952 Gdansk (Poland)
(Received April 17th, 1974; accepted for publication, July 11th, 1974)

Although literature reports on methyl ethers of *N*-glycosides are numerous[1–6], those concerning methyl ethers of *N*-acetyl-*N*-arylglycopyranosylamines are lacking. We now report on some *N*-acetyl-*N*-aryl-*O*-methyl-β-D-xylopyranosylamines (**1–9**) and -α-L-arabinopyranosylamines (**10–15**).



1 X = OMe, **2** X = Cl, **3** X = Br: $R^1 = R^2 = R^3 = OMe, R^4 = H$

4 X = OMe, **5** X = Br: $R^1 = R^3 = OMe, R^2 = OH, R^4 = H$

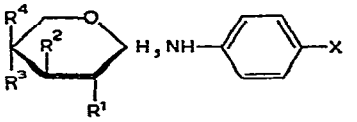
6 X = OMe, **7** X = Cl: $R^1 = OMe, R^2 = R^3 = OBz, R^4 = H$

8 X = OMe, **9** X = Cl: $R^1 = OMe, R^2 = R^3 = OH, R^4 = H$

10 X = Cl, **11** X = Br: $R^1 = R^2 = R^4 = OMe, R^3 = H$

12 X = Cl, **13** X = Br: $R^1 = R^2 = OMe, R^3 = H, R^4 = OH$

14 X = Cl, **15** X = Br: $R^1 = R^2 = OMe, R^3 = H, R^4 = AcO$



16 X = Cl, **17** X = Br: $R^1 = R^2 = R^3 = OMe, R^4 = H$

18 X = Cl, **19** X = Br: $R^1 = R^2 = R^4 = OMe, R^3 = H$

N-Acetylated *N*-*p*-methoxyphenyl-, *N*-*p*-chlorophenyl-, and *N*-*p*-bromophenyl-β-D-xylopyranosylamines[7] as well as *N*-*p*-chlorophenyl- and *N*-*p*-bromophenyl-α-L-arabinopyranosylamines[8] were methylated by the Kuhn method[9], using two equivalents of methyl iodide for each hydroxyl group. The products comprised

*Ester and Ether Derivatives of Glycopyranosylamines: Part VII. For Part VI, see Ref. 14.

mainly (70%) tri- (**1–3** and **10–11**) and di-*O*-methylated (**4** and **5**, **12** and **13**) *N*-acetyl-*N*-aryl-β-D-xylo- and -α-L-arabino-pyranosylamines, respectively.

Compounds **1**, **2**, **10**, and **11** were also obtained (~10%) by *N*-acetylation of **16**, **17**, **18**, and **19** with acetic anhydride–anhydrous sodium acetate, at ~120°. Attempts to obtain **1**, **3**, **10**, and **11** by Frèrejacque's method[10] failed. The multicomponent reaction mixtures comprised neither starting materials nor the expected products. Thus, the tri-*O*-methylated compounds differed largely from tri-*O*-acylated D-xylo- and L-arabino-pyranosylamines[7,11,12].

That HO-3 in **4** and **5** was unsubstituted was shown by a shift (~0.3 p.p.m) of the H-3 signal on methylation[13]. Similarly, comparison of the n.m.r. spectra of **10–15** suggests that HO-4 in **12** and **13** is unsubstituted.

N-Acetyl-*N*-*p*-methoxyphenyl (**6**) and *N*-acetyl-*N*-*p*-chlorophenyl (**7**) derivatives of 3,4-di-*O*-benzoyl-2-*O*-methyl-β-D-xylopyranosylamine were obtained by methylation of the 3,4-di-*O*-benzoyl derivatives[14]. Compounds **6** and **7** were *O*-debenzoylated to give **8** and **9**. The method of preparation of **8** and **9** suggests that the methoxyl group is attached to C-2 if no acyl migration had occurred. Supporting evidence for O-2 methylation was afforded by periodate oxidation (1 mol. uptake), and by the observation of only a very small change in the position of the H-2 signal in the n.m.r. spectra of compounds **1–5**, **8**, and **9**.

The coupling constants for H-1 (d, $J_{1,2}$ 8 Hz), and for H-2 and H-3 (t, $J_{2,3} \approx J_{3,4} \approx 8$ Hz, Table II) imply that, in **1–9**, H-1,2,3,4 are axial and suggest that the compounds exist in a $^4C_1$ conformation with a β-D configuration at C-1.

An α-L configuration at C-1 and a $^4C_1$ conformation for **10–15** is suggested by the nature of the signals for H-1 (d) and H-2 (t), and the coupling constants ($J_{1,2} \approx J_{2,3} \approx 9$ Hz, and $J_{3,4}$ 3 Hz, Table II) which indicate H-1,2,3 to be axial and H-4 to be equatorial. A pyranosidic structure of **1–15** is supported by the i.r. absorption bands at ~910 and 780 cm^{-1} (Table I).

The data in Table II reveal that (*1*) substitution of HO by MeO results in a diamagnetic shift (0.3–0.4 p.p.m.) of the signal of the proton attached to the relevant atom; (*2*) methylation of HO-4 is accompanied by a downfield shift of 0.2 p.p.m. of the signal for H-5*e* in **1–5** and 0.1 p.p.m. for **10–13**. Thus, $\Delta\delta$H5*e*, H5*a* for **1–5** is 0.80 p.p.m., and ~0.60 p.p.m. for *N*-acetyl-*N*-aryl-β-D-xylopyranosylamines and their ester derivatives[11]; (*3*) replacement of *eq* MeO-4 by *ax* MeO-4 results in a downfield shift of the signal for H-2 by ~0.30 p.p.m.

On the basis of the n.m.r. data published for *O*-methylated D-glucose, D-mannose, D-galactose, and other saccharide derivatives[15–17], and recorded in Table II, the signals at δ ~3.28, ~3.48, and ~3.38 for **1–5** and **8–9** have been assigned to MeO-2, MeO-3, and MeO-4, respectively.

For **10** and **11**, the signals at δ 3.26, 3.32, and 3.38 were assigned to MeO-2, MeO-3, and MeO-4, respectively, since on passing from the spectra of **1–3** (D-xylose derivatives) to those of **10** and **11** (L-arabinose derivatives), the chemical shifts of the signals for MeO-2 and MeO-4 are not likely to be changed noticeably[16,17], whereas the signal for MeO-3 should appear at a higher field[15–17] (usually 0.3 p.p.m.[15]).

TABLE I

METHYL ETHERS OF *N*-ACETYL-*N*-ARYL- AND *N*-ARYL-β-D-XYLOPYRANOSYLAMINES AND -α-L-ARABINOPYRANOSYLAMINES

Compound	Yield (%)	M.p. (degrees)	Rotation (c 0.5)		ν_{max} (cm^{-1})[a]			
			$[\alpha]_D^{20}$	[M]	C=O (ester)	C–O–C (ether)	Ring vibration	
							Asymmetric	Symmetric
1	55[b]	105–108	+80[d]	+271	—	1090vs	910m	—
2	80[b]	111–112	+80[c]	+275	—	1090vs	910m	780s
3	63[b]	88–90	+77[d]	+299	—	1095vs	915m	780s
4	10	131–132	+95[d]	+309	—	1085vs	915m	785s
5	12	114–117	+88[d]	+333	—	1090vs	915m	780s
6	80	116–118	−3[c]	−15	1720vs	1090vs	900m	—
7	85	122–125	−1[c]	−5	1725vs	1090vs	905m	775m
8	40	syrup	+68[d]	+214	—	1080vs	910m	785m
9	45	syrup	+64[d]	+202	—	1075vs	910m	780m
10	60[b]	106–108	+166[d]	+567	—	1085vs	920m	780m
11	65[b]	99–102	+102[d]	+396	—	1085vs	910m	775m
12	12	syrup	+127[d]	+419	—	1085vs	920m	780m
13	10	syrup	+109[d]	+408	—	1085vs	920m	780m
14	90	syrup	+80[d]	+297	1740vs	1095vs	905m	775m
15	85	syrup	+72[d]	+302	1740vs	1090vs	910m	780m
16	65[b]	135–136	−84[d]	−242	—	1085vs	915m	—
17	60[b]	137–138	−72[d]	−249	—	1095vs	910m	785m
18	53[b]	115–118	+152[d]	+457	—	1095vs	905m	780m
19	55[b]	134–138	+178[d]	+616	—	1085vs	910w	785m

[a]Only important bands are given. [b]Yields of methylation reaction by the Kuhn method. [c]In ethanol. [d]In chloroform. [e]Solvent system *B*.

Similarly, in the spectra of **10** and **11** and 2-*O*-methylated *N*-acetyl-*N*-aryl-α-L-arabinopyranosylamines[18], a signal due to MeO-2 of **12** and **13** occurs at $\delta \sim 3.28$, whereas that due to MeO-3 is, as expected[17], shifted upfield by ~0.10 p.p.m. (*i.e.*, $\delta \sim 3.22$). The substitution of HO-4 (**12** and **13**) by Ac (**14** and **15**) is accompanied only by a small paramagnetic shift of the signal for MeO-3.

The results show that HO-3 in *N*-acetyl-*N*-aryl-β-D-xylopyranosylamines and HO-4 in *N*-acetyl-*N*-aryl-α-L-arabinopyranosylamines are the least reactive towards methylation. The relative reactivity of the hydroxyl groups is different from that observed on esterification of the two compounds[14,18] with benzoyl chloride in pyridine.

O-Methylation of the corresponding *N*-aryl-β-D-xylopyranosylamines[7] and -α-L-arabinopyranosylamines[12] by the Kuhn method[9] gave, as the sole, identifiable products, the 2,3,4-tri-*O*-methylated derivatives **16**–**19** as crystalline, anomeric mixtures. Analogous compounds were obtained earlier by Lipták and Bognár who employed another method[4].

Compounds **16**–**19** were also obtained (in 15% yield) by *N*-deacetylation

R_F (*solvent system* A)	*Analysis* (%)						
	Molecular formula	*C*		*H*		*N*	
		Calc.	*Found.*	*Calc.*	*Found*	*Calc.*	*Found*
0.62	$C_{17}H_{25}NO_6$	60.17	60.00	7.37	7.35	4.15	4.05
0.65	$C_{16}H_{22}ClNO_5$	55.84	55.77	6.39	6.25	4.07	3.95
0.63	$C_{16}H_{22}BrNO_5$	49.48	49.30	5.67	5.53	3.60	3.50
0.30	$C_{16}H_{25}NO_6$	59.07	58.88	7.07	6.95	4.30	4.25
0.37	$C_{15}H_{20}BrNO_5$	48.12	48.07	5.34	5.20	3.74	3.58
0.60	$C_{29}H_{29}NO_8$	67.05	66.90	5.58	5.45	2.69	2.65
0.68	$C_{28}H_{26}ClNO_7$	64.00	63.85	5.33	5.17	2.66	2.58
0.42[e]	$C_{15}H_{21}NO_6$	57.87	57.70	6.75	6.70	4.50	4.42
0.45[e]	$C_{14}H_{18}ClNO_5$	53.33	53.10	5.71	5.65	4.44	4.30
0.45	$C_{16}H_{22}ClNO_5$	55.84	55.70	6.39	6.35	4.07	3.90
0.49	$C_{16}H_{22}BrNO_5$	49.48	49.32	5.67	5.48	3.60	3.65
0.22	$C_{15}H_{20}ClNO_5$	54.71	54.48	6.07	5.93	4.25	4.15
0.33	$C_{15}H_{20}BrNO_5$	48.12	47.88	5.34	5.28	3.74	3.52
0.40	$C_{17}H_{22}ClNO_6$	54.98	54.76	5.92	5.87	3.77	3.62
0.42	$C_{17}H_{22}BrNO_6$	49.03	48.78	5.28	5.03	3.36	3.20
0.73, 0.82	$C_{14}H_{20}ClNO_4$	55.70	55.98	6.68	6.66	4.64	4.39
0.75, 0.85	$C_{14}H_{20}BrNO_4$	48.55	48.26	5.82	5.72	4.05	4.15
0.68, 0.77	$C_{14}H_{20}ClNO_4$	55.70	55.15	6.68	6.66	4.64	4.50
0.64, 0.73	$C_{14}H_{20}BrNO_4$	48.55	48.45	5.82	5.85	4.05	4.20

(Zemplén) of **2**, **3**, **10**, and **11**. Attempts to obtain **15–19** by *N*-deacetylation of **2**, **3**, **10**, and **11** with methanolic dimethylamine failed, in contrast to the behaviour of *O*-acetylated *N*-acetyl-*N*-arylpentopyranosylamines[11,12,18].

EXPERIMENTAL

Melting points are uncorrected. Optical rotations were measured with a Hilger–Watt polarimeter. T.l.c. was carried out on silica gel G, using *A* carbon tetrachloride–acetone (3:1), *B* carbon tetrachloride–acetone (1:1.5). Chromatography was performed on columns of Kieselgel (<0.08 mm), using the above solvent systems. N.m.r. spectra were recorded on a Tesla-BS 487 C (80 MHz) spectrometer with Me_4Si as the internal reference. Spin decoupling was accomplished by the field-sweep technique. I.r. spectra were obtained with a Perkin–Elmer 257 spectrophotometer.

Methylation of N-*acetyl*-N-*aryl*-β-D-*xylopyranosylamines and* -α-L-*arabinopyranosylamines.* — *N*-Acetyl-*N*-aryl-β-D-xylopyranosylamines[7] and -α-L-arabinopyranosylamines[8] (0.02 mole) were methylated with *N*,*N*-dimethylformamide (60 ml),

TABLE II

P.M.R. SPECTRAL DATA[a] FOR COMPOUNDS **1–15**

Compound	*H-1*	*H-2*	*H-3*	*H-4*	*H-5e*	*H-5a*	*ΔH-5e H-5a*	$J_{1,2}$	$J_{2,3}$	$J_{4,5e}$	$J_{5e,5a}$	*MeO-2*	*MeO-3*	*MeO-4*	*NAc*	*OAc*
1	5.58d	2.60t	3.28	2.98	3.98q	3.18	0.80	10	10	3	−12	3.30	3.50	3.38	1 78	—
2	5.56d	2.60t	3.30	3.00	3.98q	3.18	0.80	9.5	9.5	3	−12	3.28	3.48	3.38	1.80	—
3	5.56d	2.60t	3.30	2.98	3.98q	3.18	0.80	9	9	3	−12	3.28	3.48	3.38	1.80	—
4	5.62d	2.62t	3.60t	3.00m	4.02q	3.20t	0.80	9.5	9.5	3	−12	3.30	—	3.36	1.80	—
5	5.60d	2.62t	3.58t	3.00m	4.00q	3.20t	0.82	9.5	9.5	3	−12	3.30	—	3.36	1.80	—
6	5.90d	3.12t	5.80t	5.00m	4.20q	3.58	0.62	10	10	3	−12	3.22	—	—	1.80	—
7	5.90d	3.10t	5.78t	5.00m	4.22q	3.60	0.62	10	10	3	−12	3.18	—	—	1.82	—
8	5.54d	2.65t	—	—	—	—	—	9	9	—	—	3.28	—	—	1.76	—
9	5.52d	2.62t	—	—	—	—	—	9	9	—	—	3.28	—	—	1.80	—
10	5.52d	2.90t	—	3.54m	4.10q	—	—	9.5	10	3	—	3.26	3.32	3.38	1.85	—
11	5.50d	2.92t	—	3.52m	4.12q	—	—	10	10	3	—	3.26	3.32	3.38	1.85	—
12	5.48d	2.88t	—	3.94m	4.00q	—	—	9	9	3	—	3.28	3.22	—	1.80	—
13	5.50d	2.90t	—	3.94m	4.00q	—	—	9.5	9.5	3	—	3.28	3.22	—	1.82	—
14	5.50d	2.86t	—	5.10m	3.90q	—	—	9.5	10	3	—	3.28	3.24	—	1.82	1.98
15	5.52d	2.88t	—	5.15m	3.90q	—	—	10	10	3	—	3.28	3.24	—	1.82	1.96

[a]Chemical shifts (p.p.m.): d doublet; m multiplet; q quartet; t triplet. Coupling constants (±0.5 Hz) were determined by first-order analysis.

0.12 mole of methyl iodide, and 0.12 mole of silver oxide at 20° for 12 h by the Kuhn method[9]. The crude, syrupy products were subjected to column chromatography (solvent *A*) to give **1–5**, and **10–13** (Table I).

Likewise, *N*-aryl-β-D-xylopyranosylamines[7] and -α-L-arabinopyranosylamines[8] were methylated, and the crude products were crystallized from ethanol to give **16–19**.

The 4-acetates (**14** and **15**) of **12** and **13** were conventionally prepared, using pyridine–acetic anhydride, and crystallised from methanol or ethanol (Table I).

N-Acetyl-N-p-*methoxyphenyl* (**6**) *and* N-*acetyl*-N-p-*chlorophenyl* (**7**) *derivatives of 3,4-di-O-benzoyl-2-O-methyl-β-D-xylopyranosylamine.* — *N*-Acetyl-3,4-di-*O*-benzoyl-*N*-*p*-methoxyphenyl-β-D-xylopyranosylamine[14] (2 mmoles) or the *p*-chloro analogue[14] was treated with methyl iodide (4 mmoles) and silver oxide (4 mmoles) in *N*,*N*-dimethylformamide. Chromatography (solvent *A*) of the crude products gave **6** and **7**.

N-Acetyl-N-p-*methoxyphenyl* (**8**) *and* N-*acetyl*-p-*chlorophenyl* (**9**) *derivatives of* 2-O-*methyl-β-D-xylopyranosylamine.* — A solution of **6** and **7** (1 mmole) and dimethylamine (15 mmoles) in 10 ml of dry methanol was stored at room temperature for 120 h. The oily, crude products were subjected to chromatography (solvent *B*) to give **8** and **9**. When oxidized in aqueous methanol solution (3:1) with sodium metaperiodate, **8** and **9** reduced 0.95 and 1.00 mol. of oxidant, respectively.

N-Acetylation of N-*aryl-2,3,4-tri*-O-*methyl*-D-*xylopyranosylamines and* -L-*arabinopyranosylamines.* — Solutions of **16–19** (5 mmoles) severally in acetic anhydride (15 ml) were refluxed at 120° with sodium acetate (2 mmoles) for 4.5 h, and then poured into ice–water. Insoluble material was dissolved in chloroform, and the solution was neutralized with a 5% aqueous sodium hydrogen carbonate, washed with water, dried (Na_2SO_4), and evaporated to leave a syrup. Chromatography (solvent *A*) gave unchanged **16–19** (80%), and **2**, **3**, **10**, or **11** (10%), respectively.

N-Deacetylation of N-*acetyl*-N-*aryl-2,3,4-tri*-O-*methyl-β-D-xylopyranosylamines* (**2–3**) *and* -α-L-*arabinopyranosylamines* (**10–11**). — To a solution of **2**, **3**, **10**, or **11** (0.5 mmole) in methanol (20 ml) was added 0.1 mmole of sodium methoxide in methanol (10 ml). The reaction mixture was heated at 65° and monitored by t.l.c. After 2.5 h, the solution was cooled, neutralized with acetic acid, and concentrated. Water was added and the solution was extracted with chloroform. The neutral, dried extract was concentrated to a syrup which was chromatographed (solvent *A*) to give unchanged **2**, **3**, **10**, or **11** (50%) and **16**, **17**, **18**, or **19** (15%, αβ-mixtures).

REFERENCES

1 J. C. IRVINE AND A. M. MOODIE, *J. Chem. Soc.*, 93 (1908) 95; J. C. IRVINE AND R. GILMOUR, *ibid.*, 93 (1908) 1429; J. C. IRVINE AND D. MCNICOLL, *ibid.*, 97 (1910) 1449; E. L. HIRST AND J. K. N. JONES, *ibid.*, (1939) 1482; G. P. ELLIS AND J. HONEYMAN, *ibid.*, (1952) 2053; R. A. LAIDLAW AND E. G. V. PERCIVAL, *ibid.*, (1949) 1600.
2 R. KUHN AND A. DANSI, *Ber.*, 69 (1936) 1745.
3 G. P. ELLIS AND J. HONEYMAN, *Advan. Carbohyd. Chem.*, 10 (1955) 95.
4 A. LIPTÁK AND R. BOGNÁR, *Acta Chim. Acad. Sci. Hung.*, 73 (1972) 335.
5 M. L. WOLFROM AND W. L. LEWIS, *J. Amer. Chem. Soc.*, 50 (1928) 837.

6 P. A. LEVENE AND R. S. TIPSON, *J. Biol. Chem.*, 101 (1933) 529.
7 J. SOKOLOWSKI AND Z. SMIATACZ, *Rocz. Chem.*, 38 (1964) 1511.
8 Z. SMIATACZ, *Carbohyd. Res.*, 34 (1974) 380.
9 R. KUHN, H. TRISCHMANN, AND I. LÖW, *Angew. Chem.*, 67 (1955) 32; *Chem. Ber.*, 90 (1957) 203.
10 M. FRÈREJACQUE, *Compt. Rend.*, 202 (1936) 1190.
11 Z. SMIATACZ, *Rocz. Chem.*, 47 (1973) 1161, 1389.
12 Z. SMIATACZ AND J. SOKOLOWSKI, *Rocz. Chem.*, 40 (1966) 1473.
13 P. C. WOLLWAGE AND P. H. SEIB, *J. Chem. Soc., C*, (1971) 3143; *Carbohyd. Res.*, 10 (1969) 589; P. A. SEIB, *ibid.*, 8 (1968) 101.
14 Z. SMIATACZ, *Carbohyd. Res.*, 38 (1974) 117.
15 E. B. RATHBONE, A. M. STEPHEN, AND K. G. R. PACHLER, *Carbohyd. Res.*, 20 (1971) 141, 357.
16 E. G. GROS, S. O. MASTRONARDI, AND A. R. FRASCA, *Carbohyd. Res.*, 16 (1971) 232.
17 E. B. RATHBONE, A. M. STEPHEN, AND K. G. R. PACHLER, *Carbohyd. Res.*, 21 (1972) 73, 83; 23 (1972) 275.
18 Z. SMIATACZ, *Rocz. Chem.*, 48 (1974) 947.