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Note

Acetolysis: the formation of acyclic by-products

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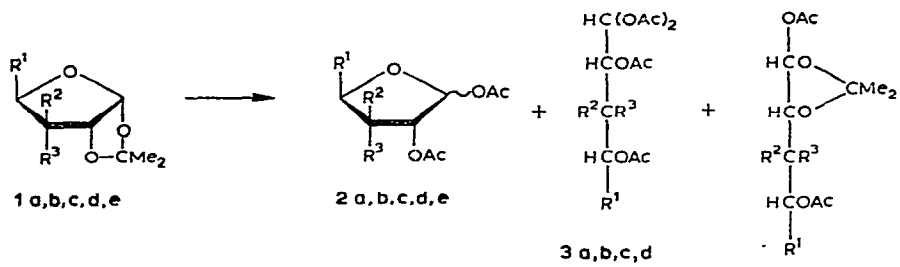
Recently, it was shown[1] that acetolysis of 3,5-di-*O*-acetyl-1,2-*O*-isopropylidene-α-D-xylofuranose (**1a**) in acetic acid–acetic anhydride, with sulphuric acid catalysis, gives acyclic by-products **3a** and **4a**, and that the formation of these products can be suppressed by decreasing the concentration of acetic anhydride. A similar study of the acetolysis of a series of related compounds has now shown that the configuration of the starting material also affects the reaction.



a $R^1 = CH_2OAc, R^2 = OAc, R^3 = H$
b $R^1 = CH_2OBz, R^2 = OMe, R^3 = H$
c $R^1 = CHOAc \cdot CH_2OAc, R^2 = OMe, R^3 = H$
d $R^1 = CH_2OBz, R^2 = H, R^3 = OMe$
e $R^1 = CH_2OAc, R^2 = H, R^3 = NHAc$

The removal of 1,2-*O*-isopropylidene groups of furanoid and pyranoid derivatives by acetolysis to give the corresponding 1,2-diacetates is an important reaction in carbohydrate chemistry[2]. The reaction is commonly carried out by using either a 10:1 mixture (Method *A*) or a 1:1 mixture (Method *B*) of acetic acid–acetic anhydride containing 3–5% of sulphuric acid (v/v). A series of furanoid compounds, namely, 5-*O*-benzoyl-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranose[3] (**1b**), 5,6-di-*O*-acetyl-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose[4] (**1c**), 5-*O*-benzoyl-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-ribofuranose[5] (**1d**), and 3-acetamido-5-*O*-acetyl-3-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose[6] (**1e**), were acetolysed using both methods at 25° over 4 days, and the results are shown in Table I.

TABLE I

YIELDS OF ACETOLYSIS PRODUCTS

Starting material	*Method*	*Yield*[a] (%)		
		Ring compound	*Aldehydrol*	Aldehydo *compound*
1b	*A*	80	15	[c]
	B	5[b]	95[b]	[c]
1c	*A*	87	2	[c]
	B	75	25	[c]
1d	*A*	85	5	[c]
	B	70	30	[c]
1e	*A*	50	[c]	4
	B	88	[c]	12

[a]The yields given for method *A* are the yields after chromatographic separation, whereas those for method *B* are determined from the H-1 signals of the n.m.r. spectra of the reaction products. [b]After 24 h, the mixture was ~1:1. [c]Not detected.

In these reactions, either an acyclic, aldehydrol derivative (**3b**, **3c**, or **3d**) or the *aldehydo* compound **4e** was obtained and, except for **2b** and **3b**, the acyclic compounds could be separated from the ring compounds. The α anomer of **2b** and the β anomers of **2d** and **2e** were obtained from the anomeric mixtures by crystallisation.

The results indicate that the acetolysis of 1,2-*O*-isopropylidene-furanose compounds with acetic acid–acetic anhydride–sulphuric acid mixtures, to obtain the corresponding 1,2-diacetates, remains a viable, preparative method, especially when the concentration of acetic anhydride is low, but that with xylofuranose derivatives, the degree of contamination increases. It should be noted that the reactions were run over 4 days, whereas a shorter reaction time is normally employed. A considerable loss of material occurs during the acetolysis of **1e** by Method *A*.

EXPERIMENTAL

M.p.'s were determined on a hot-stage apparatus. I.r. spectra were measured with a Perkin–Elmer 257 spectrophotometer, and optical rotations were measured, for solutions in chloroform, with a Bendix–NPL Automatic Polarimeter Type 143 (*c* 1.0 ±0.3). N.m.r. spectra were recorded on a Varian HA-100 instrument with tetramethylsilane as internal standard for $CDCl_3$ solutions, and mass spectra were determined with an A.E.I. MS9 spectrometer by use of the direct-insertion technique.

Method *A* refers to the use of mixtures of acetic acid and acetic anhydride (10:1) containing sulphuric acid (~5%, v/v), and Method *B* to mixtures (1:1) containing sulphuric acid (~3% v/v). After 4 days at 25°, the acetolysis mixture was

added to ice–water, stirred (2 h), and then extracted ($CHCl_3$). The combined extracts were washed with water and saturated, aqueous sodium hydrogen carbonate, until free from acid, and dried (Na_2SO_4) before evaporation; solvents were removed below 50° *in vacuo*. The syrups obtained were chromatographed on silica gel (Merck GF_{254}) or examined by n.m.r. (Method *B*).

Acetolysis of **1b**. — (*a*) *Method* A. Chromatography of the product, with chloroform–ethyl acetate (10:1) as eluant, gave a clear syrup (80%) which, on crystallisation from ethyl acetate–hexane, gave 1,2-di-*O*-acetyl-5-*O*-benzoyl-3-*O*-methyl-α-D-xylofuranose (**α-2b**, 31%) as colourless needles, m.p. 93–94°, $[\alpha]_D^{21}$ +84°, *m/e* 293 ($M^+ - CH_3CO_2$). N.m.r. data: τ 1.83–2.70 (m, C_6H_5), 3.56 (d, $J_{1,2}$ 4.5 Hz, H-1), 4.71 (t, $J_{2,1}$ 4.5, $J_{2,3}$ 5.0 Hz, H-2), 5.34–5.72 (m, H-4,5,5'), 5.85 (t, $J_{3,2}$ 5.0, $J_{3,4}$ 5.5 Hz, H-3), 6.52 (s, OMe), and 7.91, 7.93 (2s, 2 AcO).

Anal. Calc. for $C_{17}H_{20}O_8$: C, 58.0; H, 5.7. Found: C, 57.8; H, 5.6.

Evaporation of the mother liquors gave 1,2-di-*O*-acetyl-5-*O*-benzoyl-3-*O*-methyl-β-D-xylofuranose (**β-2b**) as a syrup (47%), *m/e* 293 ($M^+ - CH_3CO_2$). N.m.r. data: τ 2.91–3.70 (m, C_6H_5), 3.86 (s, H-1), 4.74 (d, $J_{2,3}$ 1 Hz, H-2), 5.24–5.58 (m, H-4,5,5'), 6.08 (q, $J_{3,4}$ 5, $J_{3,2}$ 1 Hz, H-3), 6.52 (s, OMe), and 7.89, 7.92 (2s, 2 AcO). The syrup contained ~10% of **α-2b**.

Anal. Accurate determination of mass by mass spectrometry of the base peak, $M^+ - 59$. Calc. for $C_{15}H_{17}O_6$: 293.103. Found: 293.105.

Further elution gave a colourless oil, which slowly solidified. Recrystallisation from ethyl acetate–hexane gave 1,1,2,4-tetra-*O*-acetyl-5-*O*-benzoyl-3-*O*-methyl-*aldehydo*-D-xylose aldehydrol (**3b**, 15%) as colourless needles, m.p. 79–80°, $[\alpha]_D^{21}$ +5.9°, *m/e* 395 ($M^+ - CH_3CO_2$). N.m.r. data: τ 1.59–2.72 (m, C_6H_5), 3.04 (d, $J_{1,2}$ 4 Hz, H-1), ~4.58 (m, H-4), 4.66 (t, $J_{2,1}$ 4, $J_{2,3}$ 5 Hz, H-2), 5.37 (q, $J_{5,4}$ 4, $J_{5,5'}$ 12 Hz, H-5), 5.62 (q, $J_{5',4}$ 6.5, $J_{5',5}$ 12 Hz, H-5'), 6.26 (t, $J_{3,2}$ 5, $J_{3,4}$ 5 Hz, H-3), 6.48 (s, OMe), and 7.88, 7.90, 7.95, 7.97 (4s, 4 AcO).

Anal. Calc. for $C_{21}H_{26}O_{11}$: C, 55.5; H, 5.8. Found: C, 55.4; H, 5.8.

(*b*) *Method* B. After 1 day, the reaction mixture contained **α-2b**, **β-2b**, and **3b** in the approximate ratios 2:3:6; after 4 days, the mixture consisted of only **3b** with ~5% of **β-2b**; as shown by examination of the H-1 region of their n.m.r. spectra.

Acetolysis of **1c**. — (*a*) *Method* A. Chromatography of the product with chloroform–ethyl acetate (9:1) as eluant gave 1,2,5,6-tetra-*O*-acetyl-3-*O*-methyl-α,β-D-glucofuranose (**2c**), 85% as a colourless syrup, *m/e* 362 (M^+). N.m.r. data: the spectrum was as expected, and signals at τ 3.62 (d, $J_{1,2}$ 4 Hz, H-1α) and 3.89 (s, H-1β) indicated that the α:β anomeric mixture was ~1:5.

Anal. Accurate determination of mass by mass spectrometry of the base peak, $M^+ - 59$. Calc. for $C_{13}H_{29}O_8$: 303.108. Found: 303.109.

Further elution gave a mixture of **β-2c** and hexa-*O*-acetyl-3-*O*-methyl-*aldehydo*-D-glucose aldehydrol (**3c**, 4%) as a clear syrup, *m/e* 405 ($M^+ - CH_3CO_2$). N.m.r. data: the spectrum was as expected, and signals at τ 3.07 (d, $J_{1,2}$ 4.5 Hz, H-1 of the aldehydrol) and 3.89 (s, H-1β) indicated that the mixture was ~1:1 (aldehydrol:β-anomer).

Anal. Accurate determination of mass by mass spectrometry of the base peak, $M^+ - 59$. Calc. for $C_{17}H_{25}O_{11}$: 405.140. Found: 405.138.

(*b*) *Method* B. After 4 days, the reaction mixture contained ~25% of **3c**.

Acetolysis of **1d**. — (*a*) *Method* A. Chromatography of the product with ethyl acetate–hexane (1:3) as eluant gave a clear syrup (85%) which slowly solidified. Recrystallisation from ethyl acetate–hexane gave 1,2-di-*O*-acetyl-5-*O*-benzoyl-3-*O*-methyl-β-D-ribofuranose (**β-2d**, 63%) as needles, m.p. 67–68°, $[\alpha]_D^{21}$ −17°, *m/e* 352 (M^+). N.m.r. data: τ 1.89–2.68 (m, C_6H_5), 3.86 (s, H-1), 4.68 (d, $J_{1,2}$ 4 Hz, H-2), 5.2–6.01 (m, H-3,4,5,5'), 6.61 (s, OMe), and 7.77, 8.09 (2s, 2 AcO).

Anal. Calc. for $C_{17}H_{20}O_8$: C, 58.0; H, 5.6. Found: C, 58.2; H, 5.8.

N.m.r. spectroscopy of the syrup obtained on evaporation of the mother liquors showed that it contained no α anomer (**α-2d**); it did, however, contain a small amount of the aldehydrol (**3d**).

Further elution gave 1,1,2,4-tetra-*O*-acetyl-5-*O*-benzoyl-3-*O*-methyl-*aldehydo*-D-ribose aldehydrol (**3d**) as a clear syrup (5%), $[\alpha]_D^{21}$ +10°, *m/e* 395 ($M^+ - CH_3CO_2$). N.m.r. data: τ 1.95–2.59 (m, C_6H_5), 2.94 (d, $J_{1,2}$ 5 Hz, H-1), 4.54–4.70 (m, H-2,4), 5.36 (q, $J_{5,5'}$ 10, $J_{5,4}$ 3 Hz, H-5), 5.60 (q, $J_{5',5}$ 10, $J_{5',4}$ 6 Hz, H-5'), 6.35 (t, $J_{3,2}$ 5, $J_{3,4}$ 5 Hz, H-3), 6.53 (s, OMe), and 7.87, 7.89, 7.92, 7.96 (4s, 4 AcO).

Anal. Accurate determination of mass by mass spectrometry of the base peak, $M^+ - 59$. Calc. for $C_{19}H_{23}O_9$: 395.134. Found: 395.132.

(*b*) *Method* B. After 4 days, the reaction mixture contained ~30% of **3d**.

Acetolysis of **1e**. — (*a*) *Method* A. Work-up of the reaction mixture gave a clear syrup which slowly crystallised. Recrystallisation from ethyl acetate–hexane gave **β-2e** (41%) as needles, m.p. 102–103°; lit.[6] m.p. 102–103°. The mother liquors were concentrated, and chromatography with ethyl acetate as eluant gave a colourless oil which slowly crystallised. Recrystallisation from ethyl acetate–hexane gave 3-acetamido-1,4,5-tri-*O*-acetyl-3-deoxy-1,2-*O*-isopropylidene-*aldehydo*-D-ribose (**4e**) as needles (4%), m.p. 100–101°, $[\alpha]_D^{19}$ +59°, *m/e* 360 ($M^+ - CH_3$). N.m.r. data: τ 3.65 (d, $J_{NH,3}$ 9 Hz, disappears on addition of D_2O, NH), 3.75 (d, $J_{1,2}$ 2.5 Hz, H-1), 4.75 (m, $J_{4,3}$ 6, $J_{4,5}$ 6, $J_{4,5'}$ 3.5 Hz, H-4), 5.46 (m, $J_{3,NH}$ 9, $J_{3,2}$ 6, $J_{3,4}$ 6 Hz, simplifies on addition of D_2O, H-3), 5.58–5.90 (m, H-2,5,5'), 7.91, 7.93, and 7.99 (3s, 3 AcO and NHAc), and 8.53 (s, CMe_2).

Anal. Calc. for $C_{16}H_{25}NO_9$: C, 51.2; H, 6.7; N, 3.7. Found: C, 51.2; H, 6.8; N, 3.6.

Further elution gave **2e** as a clear syrup (9%), *m/e* 258 ($M^+ - CH_3CO_2$). N.m.r. data: the spectrum was as expected, and signals at τ 3.57 (d, $J_{1,2}$ 4 Hz, H-1α) and 3.89 (s, H-1β) indicate that the ratio of anomers was ~1:1.

Anal. Accurate determination of mass by mass spectrometry of the base peak, $M^+ - 59$. Calc. for $C_{11}H_{16}NO_6$: 258.254. Found: 258.255.

(*b*) *Method* B. After 4 days, the reaction mixture contained ~12% of **4e**.

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