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Note

Cyclic monothioacetals of aldoses: synthesis and desulphuration of 2-polyacetoxyalkyl-1,3-oxathiolan-5-ones and -3,1-benzoxathian-4-ones*

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Actithiazic acid (acidomycin, mycobacidin, cinnamonin, thiazolidone antibiotic PA-95, **1**) is an acid-stable antibiotic produced by certain streptomycetes (*S. virginiae*, *S. acidomyceticus*, *S. roseochromogenes*, and *S. lavendulae*)[1–3], which is active against mycobacteria *in vitro* because it reduces the synthesis of biotin. From the point of view of activity, it is important to have a side chain of optimum length bearing the terminal carboxyl group[4]. The only known carbohydrate derivatives of this antibiotic are 6-(thiazolidin-4-on-2-yl)hexanoylhydrazones of D-glucose and D-fructose[5].

In order to obtain carbohydrate analogues (**2**) of **1**, mercaptoacetamide was reacted with 2,3,4,5,6-penta-*O*-acetyl-D-galactose (**5b**). Instead of the expected thiazolidinone derivative [**2b**, R = $(CHOAc)_4CH_2OAc$], however, a nitrogen-free product was obtained. On the basis of elemental analysis data as well as the presence of an i.r. band at 1787 cm^{-1} (indicating a 5-membered lactone ring), the 1,3-oxathiolan-5-one structure **3b** was suggested. It is known that a suitably placed hydroxyl[6] or mercapto[7,8] group may catalyse the cleavage of an *N*-acyl bond. The same product (**3b**) was obtained from **5b** by reaction with mercaptoacetic acid. Desulphuration of **3b** with Raney nickel gave the expected hexa-*O*-acetylgalactitol (**6b**). Similarly, the acetylated *aldehydo*-forms of D- and L-arabinose, D-glucose, and D-mannose (D- and L-**5a**, **5c**, and **5d**) were also transformed into the corresponding oxathiolanone derivatives (D-**3a**, L-**3a**, **3c**, and **3d**), each of which had a characteristic i.r. band at 1780–1790 cm^{-1}. The reaction of 2,3,4,5,6-penta-*O*-acetyl-D-mannose (**5d**) gave two main products (**3d** diastereoisomers), as well as a minor component (4%) which had the same content of sulphur as **3d**, but only an ester band (1758–1735 cm^{-1}) in the 2900–1500 cm^{-1} i.r. region.

Cyclocondensation of **5b** with 2-mercaptobenzoic acid gave the diastereoisomeric 3,1-benzoxathian-4-ones (−)- and (+)-**4b**. The structure assignment was

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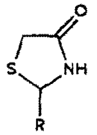
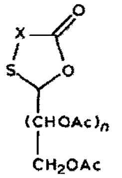


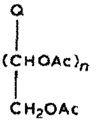
1 R = $(CH_2)_5CO_2H$

2 R = $(CHOR')_nCO_2R''$



3 X = CH_2

4 X = 1,2-C_6H_4



5 Q = CHO

6 Q = CH_2OAc

7 Q = CH_2OBz

a *arabino* (n = 3)
b D-*galacto* (n = 4)
c D-*gluco* (n = 4)
d D-*manno* (n = 4)

corroborated by desulphuration, which gave 2,3,4,5,6-penta-*O*-acetyl-1-*O*-benzoyl-D-galactitol (**7b**). This method may find general application for the preparation of compounds of type **7**.

EXPERIMENTAL

General method for the preparation of 2-polyacetoxyalkyl-1,3-oxathiolan-5-ones (**3a–d**). — A solution of the acetylated *aldehydo*-aldose (**5a–d**, 3 mmol) in hot benzene (20–50 mL) was gently boiled for 15–30 min under a small Vigreux column for the azeotropic removal of water; then, after the addition of the mercapto-carboxylic acid (3.2 mmol), the heating was continued under nitrogen for 5–7 h. The mixture was cooled, and the product was collected and recrystallised. If no product separated, the cold mixture was washed with aqueous $NaHCO_3$ and water, treated with $MgSO_4$, fuller's earth, and charcoal, and then concentrated (under diminished pressure), and the residue was recrystallised.

For the preparation of L-**3a** and **3b**, ~30 min after the addition of mercapto-acetic acid, acetic anhydride–benzene (1:2, 15–20 mL) was gradually introduced. The product was then isolated as described above.

*2-(*D-galacto*-Penta-acetoxypentyl)-3,1-benzoxathian-4-one* (**4b**). — Under the above conditions, 2-mercaptobenzoic acid (3 mmol) was added to a hot solution of **5b** (3 mmol) in benzene (20 mL). After further heating (30 min) under nitrogen, anhydrous toluene-*p*-sulphonic acid (5–10 mg) was added. The mixture was heated (9 h) and processed, as described above, to give the (−)- and (+)-diastereoisomers of **4b** (see Table I).

General method for the desulphuration. — Raney nickel (6–8 g) was rinsed with water and several times with anhydrous ethanol and then added to a hot solution of the monothioacetal (0.4 g) in anhydrous ethanol (40–80 mL). The mixture was heated on a water bath for 3–4 h with occasional shaking and then filtered hot, the filtrate was treated with charcoal and then concentrated (under diminished pressure), and the residue was recrystallised (see Table I).

TABLE I

PHYSICAL DATA OF D-**3a**, L-**3a**, **3b–d**, (−)-**4b**, (+)-**4b**, **6b**, AND **7b**

Com-pound	*Yield (%)*[a]	*M.p. (degrees)*[b] *(Solvent of recrystallisation)*	$[\alpha]_D^{23}$[c] *(degrees)*	*Formula*	*Analysis Found (calc.)*	$\nu_{lactone}$[d] *(cm⁻¹)*	*δ (p.p.m.)*[e]	
							O–CHR-S	*CH₂S*
D-**3a**	32	155 (Me$_2$CO–Et$_2$O–hexane)	+55	$C_{15}H_{20}O_{10}S$	C, 46.33 (45.91); H, 5.15 (5.14); S, 8.26 (8.17)	1790		
L-**3a**	41	156 (Me$_2$CO–Et$_2$O–hexane)	−55	$C_{15}H_{20}O_{10}S$	C, 45.90 (45.91); H, 5.13 (5.14); S, 8.11 (8.17)	1790		
3b	58	234–236 (EtOH)	+46	$C_{18}H_{24}O_{12}S$[f]	C, 46.39 (46.54); H, 5.22 (5.21); S, 6.78 (6.90); Ac, 48.71 (46.34)	1787	5.32[g] (s)	3.64[h] (AB m, 2 H)
3c	43	129 (Me$_2$CO–Et$_2$O–hexane)	−15	$C_{18}H_{24}O_{12}S$	C, 46.45 (46.54); H, 5.25 (5.21); S, 6.76 (6.90)	1783	[g]	3.79[i] (AB m, 2 H)
3d	9[j]	121 (Me$_2$CO–Et$_2$O–hexane)	+13	$C_{18}H_{24}O_{12}S$	C, 46.78 (46.54); H, 5.34 (5.21); S, 6.89 (6.90)	1787	[g]	3.75[k] (s, 2 H)
	19[j]	103.5 (Et$_2$O–hexane)	+77		C, 46.59 (46.54); H, 5.20 (5.21); S, 6.90 (6.90)	1790	5.60[g] (s)	3.66[l] (AB m, 2 H)
4b	24	206 (EtOAc)	−25	$C_{23}H_{26}O_{12}S$	C, 52.70 (52.46); H, 4.97 (4.98); S, 6.02 (6.09)	1760–1740[m]	5.62[g] (s)	
	30	182 (EtOAc–hexane)	+73		S, 6.05 (6.09)	1756–1740[m]	5.62[g] (d, *J* <2 Hz)	
6b[n,o]	44	168[p] (EtOH)		$C_{18}H_{26}O_{12}$				
7b[q]	31[r]	160 (EtOH)		$C_{23}H_{28}O_{12}$	C 55.76 (55.64); H, 5.70 (5.68)			
	38[s]	160 (EtOH)						

[a] For general methods of preparation, see Experimental. [b] Melting points are uncorrected and were determined on a Kofler block. [c] In chloroform (*c* 1), measured with a Schmidt-Haensch visual polarimeter (1-dm pathlength). [d] Recorded with a Unicam SP-200 spectrophotometer (KBr discs). [e] 100-MHz ^{1}H-n.m.r. spectra were recorded with a JEOL JNM-100 spectrometer for solutions in CDCl$_3$ (internal Me$_4$Si). [f] Mol. wt., determined using a thermistoric osmometer for a solution in chloroform, was 460 (calc., 464.46). [g] Among the signals for H-2,3,4,5 of the hexose. [h] δ 4.40–3.80 (ABX m, 2 H, CH$_2$O). [i] δ 4.50–4.16 (ABX m, 2 H, CH$_2$O). [j] After purification by column chromatography (silica gel, 6:1 benzene–EtOAc). A third product was also isolated (4%); m.p. 199° (from acetone–hexane), $[\alpha]_D^{23}$ +72° (*c* 1, chloroform), no lactone band at 1780–1790 cm^{-1}. ^{1}H-N.m.r. data: δ 6.03 (s, 1 H, O–CHR–S), 5.72–4.48 (m, 4 H, H-2,3,4,5 of the hexose), 4.48–4.12 (ABX m, 2 H, CH$_2$O), 3.47 (AB m, 2 H, CH$_2$S), 2.20–2.12 (5 Ac). *Anal.* Calc. for $C_{18}H_{24}O_{12}S$: S, 6.90. Found: S, 7.08. [k] δ 4.38–3.97 (ABX m, 2 H, CH$_2$O). [l] δ 4.36–3.97 (ABX m, 2 H, CH$_2$O). [m] $\nu_{C=O}$ band of OAc including that of the lactone. [n] By the desulphuration of **3b** (see Experimental). [o] Identical (t.l.c., i.r. spectrum) with an authentic specimen. [p] Lit.[9] m.p. 168–169° (from ethanol). [q] The i.r. spectra of **7b** obtained both from (−)- and (+)-**4b** were identical: 1750–1735 and 1731 (sh) (ester), 1600 and 1582 (Ar), 710 and 670 cm^{-1} (monosubstituted phenyl). ^{1}H-N.m.r. data: δ 7.94–7.84 (m, 2 H, H-Ar), 7.49–7.22 (m, 3 H, H-Ar), 5.52–5.22 (m, 4 H, H-2,3,4,5 of hexose), 4.46–3.64 (m, 4 H, 2 CH$_2$), 2.11–2.00 (15 H, 5 Ac). [r] By the desulphuration of (−)-**4b**. [s] By the desulphuration of (+)-**4b**.

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