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Preliminary communication

Preparation of 2-deoxy-β-D-*lyxo*-hexosides (2-deoxy-β-D-galactosides)

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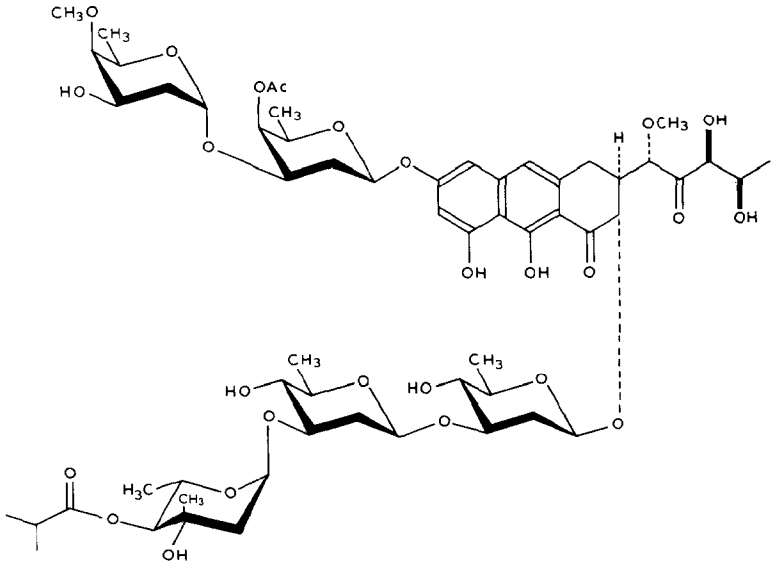
With a view to the eventual synthesis of the trisaccharide chain of the antitumor antibiotic olivomycin A[1] (**1**), we have studied the preparation[2] of heptulosonic acid *O*-glycosides and their stereoselective radical decarboxylation[3] to 2-deoxy-β-D-*arabino*-hexosides (2-deoxy-β-D-glucosides). We now report the preparation of 2-deoxy-β-D-*lyxo*-hexosides (2-deoxy-β-D-galactosides), relevant to the disaccharide chain of olivomycin A, and improvements in the synthesis of heptulosonic acids.



1 Olivomycin

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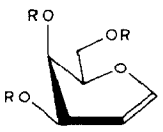
Treatment of D-galactal[4] with 3.5 equiv. of *tert*-butyldimethylsilyl chloride and 7 equiv. of imidazole in *N,N*-dimethylformamide at 60° for 2 days gave 86% of the D-galactal derivative **2**† as a colourless oil, $[\alpha]_D^{25} = -37°$ (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 6.22 (d, 1 H, $J_{1,2}$ 7 Hz, H-1), 4.65 (m, 1 H, H-2). Reaction of **2** with 1 equiv. of hydrogen chloride in toluene at 0°, and subsequently with 1.3 equiv. of thiophenol and 1.3 equiv. of ethyldi-isopropylamine in dichloromethane at 25°, afforded 76% of the thioglycoside **3**, after chromatography on silica gel, as a 1:14 $\alpha\beta$-mixture. ^{1}H-N.m.r. data ($CDCl_3$): β anomer, δ 4.74 (dd, 1 H, $J_{1,2e}$ 2.2, $J_{1,2a}$ 11.9 Hz, H-1); α anomer, δ 5.62 (d, 1 H, *J* 4.8 Hz, H-1). Alternatively, the camphor-10-sulphonic acid-catalysed reaction of **2** with 4 equiv. of thiophenol in dichloromethane in the presence of powdered molecular sieves gave 60% of **3** isolated as a 15:1 $\alpha\beta$-mixture.

Oxidation of crude **3** (obtained by the former procedure) with 2.4 equiv. of 3-chloroperoxybenzoic acid in dichloromethane at 0° in the presence of sodium hydrogencarbonate gave the corresponding sulphone **4** (67% from **2**). ^{1}H-N.m.r. data ($CDCl_3$): β anomer, δ 4.45 (dd, 1 H, $J_{1,2e}$ 2, $J_{1,2a}$ 12 Hz, H-1); α anomer, δ 4.78 (dd, 1 H, *J* 2.2 and 6.3 Hz, H-1). The sulphone **4** was obtained (96%) by oxidation of pure **3** with 1.05 equiv. of commercial magnesium monoperoxyphthalate[5] in ethanol at 5°. Sequential treatment of **4** in tetrahydrofuran at −70° with a solution of butyl-lithium (1.2 equiv.), dimethyl carbonate (1.3 equiv.), a solution of lithium naphthalenide (2.5 equiv.) in tetrahydrofuran, and diphenyl disulphide (2.0 equiv.),



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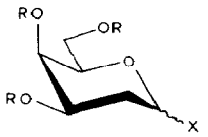
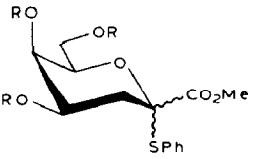


3 X = SPh
4 X = SO_2Ph



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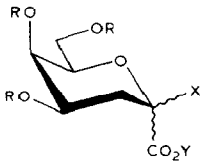
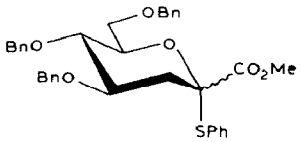


7 X = OMe, Y = Me
8 X = O-4-cresyl, Y = Me
9 X = O-3β-cholestanyl, Y = Me
10 X = SPh, Y = H
11 X = OMe, Y = H
12 X = O-4-cresyl, Y = H
13 X = O-3β-cholestanyl, Y = H

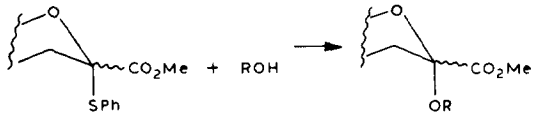


6

R = ^{t}BuMe$_2$Si

†All new products gave satisfactory spectroscopic and microanalytical data (C,H ±0.4%). With the exception of **5**, all of the new compounds were isolated as syrups.

Table I

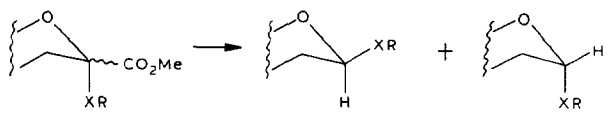


Alcohol	Coupling agent	Product (%)
MeOH	$HgCl_2$	7 (67)
4-Cresol	$HgCl_2$	8 (54)
3β-Cholestanol	NBS	9 (39)

followed by aqueous work-up and chromatography on silica gel (ether–light petroleum 1:19), gave 63% of methyl [phenyl 4,5,7-tri-*O*-(*tert*-butyldimethylsilyl)-3-deoxy-2-thio-D-*lyxo*-2-heptulopyranosid]onate (**5**) as an 8:1 αβ-mixture, m.p. 99–100° (from ether–light petroleum). ^{1}H-N.m.r. data ($CDCl_3$): α anomer, δ 2.39 (dd, 1 H, H-2*a*) and 2.14 (dd, 1 H, H-2*e*). The above procedure gave significantly better yields of **5** than when the intermediates were isolated and purified.

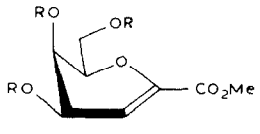
Compound **5** was coupled with alcohols using *N*-bromosuccinimide, mercuric acetate, or mercuric chloride as the activating agent, as described for the glycosyl donor **6**. Thus, storage of a mixture of **5**, alcohol (2 equiv.), powdered molecular sieves, and the activating agent (1.1 equiv.) at room temperature gave, after chromatography, the corresponing 2-deoxy-α,β-galactosides **7–9** (see Table I). The unsaturated ester **14** was a minor product of these reactions. ^{1}H-N.m.r. data ($CDCl_3$): δ 5.83 (d, 1 H, *J* 3.2 Hz, H-2). Saponification of the esters **5** and **7–9** afforded the corresponding acids (**10–13**) which were not purified but decarboxylated by reaction with 3-oxa-2-oxo-1-thiaindolizinium chloride[6] (**15**) and triethylamine in dichloromethane, followed by photolysis of the resulting *O*-acyl thiohydroxamates[7], in the presence of *tert*-dodecanethiol. For example, the ester **8** was saponified with aqueous potassium hydroxide (1.5 equiv.) in methanol–tetrahydrofuran and the crude acid **12** was obtained by extraction with ether after acidification to pH 2. Treatment of **12** in dichloromethane with the salt **15** (1 equiv.) in the presence of powdered molecular sieves at 20° under nitrogen for 5 min,

Table II



Ulosonate ester	Product (%)	αβ-Ratio
5	3 (48)	1 : 18
7	16 (55)	1 : 10
8	17 (34)	1 : 16
9	18 (44)	1 : 8

followed by the addition of triethylamine (1 equiv.), gave the yellow thiohydroxamate which was treated with *tert*-dodecanethiol (5 equiv.) and irradiated for 1.5 h with a 500-W tungsten lamp under nitrogen at 5°. Chromatography of the product gave 34% of the 4-cresyl galactoside **17** with a 1:16 $\alpha\beta$-ratio. ^{1}H-N.m.r. data ($CDCl_3$): β anomer, δ 4.99 (dd, 1 H, $J_{1,2e}$ 2.3, $J_{1,2a}$ 9.8 Hz, H-1). The results of the radical decarboxylation reactions are given in Table II. Each of the 2-deoxy-D-galactosides (**3**, and **16–18**) had good β-selectivities, demonstrating that the new method for their preparation tolerates both axial and equatorial 4-substituents.



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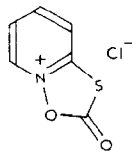
R = ^{t}BuMe$_2$Si



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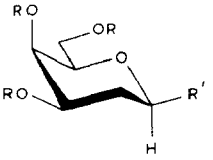

16* R′ = OMe
17* R′ = O-4-cresyl
18* R′ = O-3β-cholestanyl
*Major isomet only represented

ACKNOWLEDGMENTS

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