DECILONITROSE AND 4-*O*-SUCCINYL-L-DIGINOSE, SUGAR COMPONENTS OF DECILORUBICIN

Sir:

Decilorubicin,[1] a new anthracycline antibiotic produced by *Streptomyces virginiae* MF-266-g4 yields three kinds of sugars on hydrolysis. As reported in a previous paper,[1] hydrogenolysis of decilorubicin methyl ester gave rhodosamine. Two other sugar components have been obtained as their methyl glycosides by methanolysis of decilorubicin. One of them, a new nitro sugar is named decilonitrose. In this communication their structures and syntheses are reported.

Methanolysis of decilorubicin (2.0 g) in 0.5 M methanolic HCl (200 ml) at 70°C for 4.5 hours followed by column chromatography on silica gel developed with mixtures of 50: 1, 30: 1, and 6: 1 of toluene and ethyl acetate, successively, gave three methyl glycosides as colorless syrupy solids: a new nitro sugar, methyl β-decilonitroside [**1**, 28 mg, easily sublimes under a reduced pressure, $[\alpha]_D^{23}$ −13° (*c* 0.2, chloroform), IR: 1540 cm^{-1} (NO_2); MS: *m/z* 159 ($M-NO_2$)], methyl 4-*O*-succinyl-α-L-diginoside methyl ester [**2**, 127 mg, $[\alpha]_D^{23}$ −129° (*c* 1.0, chloroform)] and the β-anomer of **2** [**3**, 37 mg, $[\alpha]_D^{23}$ −0.1° (*c* 0.1, chloroform)]. The ^1H NMR chemical shifts of **1** and ^{13}C NMR chemical shifts of **1**, **2** and **3** are shown in Tables 1 and 2, respectively.

By spectral analysis, the structure of **1** was suggested to be methyl 2,3,6-trideoxy-3-*C*-methyl-

Table 1. ^1H NMR chemical shifts and coupling constants for methyl glycosides **1** and **4**.

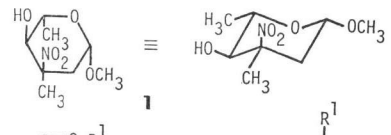
Proton	**1**		**4**	
	δ, ppm	*J*, Hz	δ, ppm	*J*, Hz
1	4.51 dd	2.0, 9.4	4.81 m	1.5~2, 1.5~2
2ax	1.77 dd	9.4, 15.0	1.8~2.0	
2eq	2.74 dd	2.0, 15.0		
3			3.61 m	6.4, 11.2
4	3.1~3.3		3.78 d	3.0
5	3.69 m	6.0, 9.0	3.83 q	6.8
6	1.39 d	6.0	1.32 d	6.8
3-CH_3	1.73 s			
OCH_3	3.48 s		3.33 s	
OCH_3			3.39 s	

The ^1H NMR spectra were taken with a Bruker WM250 spectrometer in $CDCl_3$.

Table 2. ^{13}C NMR chemical shifts of methyl glycosides.

Carbon	**1**	**2**	**3**	**4**	**8**
1	98.6 d	98.9 d	101.2 d	98.7 d	99.1 d
2	41.7 t	31.0 t	32.8 t	29.4 t	41.4 t
3	89.6 s	64.8* d	67.9* d	65.5* d	89.3 s
4	77.0 d	69.0* d	69.4* d	67.8* d	74.6 d
5	71.1 d	73.4* d	76.8* d	74.8* d	70.5 d
6	18.3 q	16.8 q	16.7 q	16.8 q	18.3* q
3-CH_3	25.2 q				18.1* q
OCH_3	56.5 q	56.2 q	56.5 q	55.6 q	56.5 q
OCH_3		54.9 q	56.5 q	54.8 q	
Ester CH_3		51.8 q	51.8 q		
C=O		172.5 s	172.5 s		
C=O		172.1 s	172.2 s		
CH_2		29.3 t	29.2 t		
CH_2		29.2 t	29.1 t		

The ^{13}C NMR spectra were taken with a Varian XL-100 spectrometer in $CDCl_3$ and chemical shifts (ppm) referred to Me_4Si as the internal standard. Values with asterisks within each column may be interchanged. Assignments (s, d, t and q) show off-resonance multiplicities.



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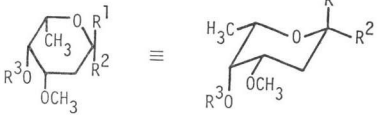
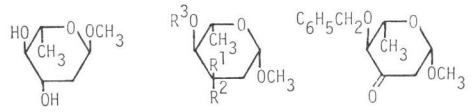


	R^1	R^2	R^3
2	OCH_3	H	$COCH_2CH_2COOCH_3$
3	H	OCH_3	$COCH_2CH_2COOCH_3$
4	OCH_3	H	H

3-nitro-β-L-*ribo*-hexopyranoside (methyl 4-*O*-demethyl-3-*epi*-β-evernitroside) or its β-D-isomer. The former structure was confirmed for **1** by chemical synthesis, as described later.

Methanolysis of **2** with 0.68% sodium methoxide in methanol overnight at room temperature gave methyl α-L-diginoside (**4**), $[\alpha]_D^{23}$ $-159.1°$ (*c* 1.0, chloroform) [Reference 2: $[\alpha]_D^{20}$ $-70°$ (*c* 0.5, chloroform)] and dimethyl succinate which was identified by gas chromatography. The ^1H and ^{13}C NMR chemical shifts of **4** are shown in Tables 1 and 2, respectively. Hydrolysis of **4** with 0.05 M H_2SO_4 in 50% aqueous dioxane in a sealed tube at 90°C for 3.5 hours gave L-diginose, $[\alpha]_D^{22}$ $-66.5°$ (*c* 0.2, water, after 24 hours) [Reference 3: $[\alpha]_D^{25}$ $-64.7° \pm 5°$ (*c* 0.4, water, after 17 hours)]. Compounds **2** and **4** have been synthesized in order to solve the difference with the optical rotation value of **4** in reference 2 as described later.

Methyl 2,6-dideoxy-β-L-*arabino*-hexopyranoside[4] (**5b**) which was synthesized starting from L-rhamnose through 1,5-anhydro-3,4-di-*O*-acetyl-2,6-dideoxy-L-*arabino*-hex-1-enitol (3,4-di-*O*-acetylrhamnal)* was acylated with benzoyl chloride in pyridine at $-50°$C for 1 hour to yield preferentially the 3-*O*-benzoate (**6**) in 71% yield, $[\alpha]_D^{24}$ $+26.8°$ (*c* 1.0, chloroform). *O*-Benzylation of **6** with benzyl bromide and NaH in *N*, *N*-dimethylformamide at 0°C for 30 minutes followed by deacylation with sodium methoxide in methanol at room temperature for 4 hours



	R^1	R^2	R^3
5a			
5b	H	OH	H
6	H	$OCOC_6H_5$	H
7	H	OH	$CH_2C_6H_5$
8	CH_3	NO_2	H
9	NH_2	CH_3	H
10	CH_3	NH_2	H
12	CN	OSO_2CH_3	$CH_2C_6H_5$
13	OSO_2CH_3	CN	$CH_2C_6H_5$

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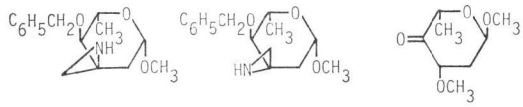

14 **15** **16**

gave colorless crystals of the 4-*O*-benzyl ether (**7**) in 56% yield, mp 108°C, $[\alpha]_D^{24}$ $+83.0°$ (*c* 0.2, chloroform).

By the synthetic route of YOSHIMURA *et al.*[5] for evernitrose and 3-*epi*-evernitrose, **1** and its 3-epimer (**8**) were synthesized from **7** through methyl 3-amino-2,3,6-trideoxy-3-*C*-methyl-β-L-*ribo*- (**9**) and -*arabino*-hexopyranoside (**10**), respectively. Oxidation of **7** with CrO_3-pyridine in dichloromethane gave the 3-ulose (**11**) in 73% yield, mp 83~85°C, $[\alpha]_D^{24}$ $-108°$ (*c* 1.0, chloroform). Cyanomesylation of **11** by successive reaction of HCN and methanesulfonyl chloride followed by column chromatography on silica gel developed with a mixture of hexane and ethyl ether (3:1) gave the 3-cyano-3-*O*-mesyl derivatives having L-*arabino* [**12**, 42% yield, mp 109°C, $[\alpha]_D^{22}$ $-16.2°$ (*c* 0.5, dichloromethane)] and L-*ribo* [**13**, 33% yield, syrupy, $[\alpha]_D^{22}$ $-22.8°$ (*c* 0.5, chloroform)] configurations. Compounds **12** and **13** were reduced with $LiAlH_4$ to give the spiro-aziridine derivatives **14** and **15**, which were hydrogenated with Raney Ni catalyst to yield the 3-amino-3-methyl derivatives having L-*ribo* [**9**, 55% yield from **12**, $[\alpha]_D^{23}$ $+45.6°$ (*c* 1.0, chloroform), MS: *m/z* 176 $(M+1)^+$] and L-*arabino* [**10**, 43% yield from **13**, $[\alpha]_D^{23}$ $+33.3°$ (*c* 1.0, chloroform), MS: *m/z* 176 $(M+1)^+$] configurations, respectively. The difference in the configurations of **9** and **10** were examined by the TACu method:[6] **9** showed positive contribution $[\Delta[M]_{436(TACu)}$ $+525°]$ and **10** showed negative

* Treatment of 3,4-di-*O*-acetylrhamnal with Br_2 in dichloromethane, and subsequent reaction with methanol and Ag_2CO_3, followed by hydrogenation with Pd-C in a mixture of methanol, water and triethylamine (5:4:1) in a Parr apparatus (3.5 kg/cm^2) afforded α-anomer (**5a**, 16% yield) and β-anomer (**5b**, 49% yield).[4,5]

[$\Delta[M]_{436(TACu)}$ −621°]. Thus, the absolute configurations of **9** and **10** have been determined, and **9** is the desired compound for synthesis of **1**.

Oxidation of **9** with *m*-chloroperbenzoic acid in acetonitrile at room temperature for 1 hour followed by preparative TLC on silica gel plates developed with dichloromethane gave **1** (29% yield), which was identical with the natural **1** derived from decilorubicin in all respects. Therefore, the structure of **1** was determined to be methyl 2,3,6-trideoxy-3-*C*-methyl-3-nitro-β-L-*ribo*-hexopyranoside. The β-L-*arabino* isomer [**8**, a colorless syrupy solid, $[\alpha]_D^{25}$ +41.7° (*c* 1.0, chloroform, MS: *m/z* 205 (M^+)] was also synthesized from **10** in 62% yield. The ^{13}C NMR chemical shift of the 3-axial methyl carbon in **8** is at higher field than that of the 3-equatrial carbon in **1**,[7] as shown in Table 2.

Methyl α-L-diginoside (**4**) was synthesized from **5a** through the 4-ulose[2] (**16**) in seven steps. Reduction of **16** with the "ate" complex[8] generated from diisobutylaluminium hydride and *n*-butyllithium in ethyl ether at room temperature for 30 minutes gave stereospecifically **4** (79% yield) which was identical with the natural **4** in all respects including the optical rotation value, $[\alpha]_D^{24}$ −158° (*c* 1.0, chloroform).* Acylation of **4** with succinic anhydride in dichloromethane in the presence of *N,N'*-diisopropylethylamine under refluxing for 5 hours followed by esterification with diazomethane in ethyl ether at room temperature for 1 hour gave **2**, which was identical with the natural **2** derived from decilorubicin in all respects.

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* The optical rotation value of **4** in the reference 2 should be corrected.

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