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Note

Preparation and anthelmintic activity of D-glycopyranosylidene acetals*

KATSUJI ASANO**, SHIGEOMI HORITO, JUJI YOSHIMURA†,
Laboratory of Chemistry for Natural Products, Tokyo Institute of Technology, Nagatsuta, Midoriku, Yokohama 227 (Japan)

TADASHI NAKAZAWA, ZEN-ICHIRO OHYA, AND TETSUO WATANABE
Research Laboratory, Meiji Seika Kaisha, Ltd., Kohokuku, Yokohama 222 (Japan)
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Antibiotics of the orthosomycin family[1] include a unique type of acetal interlinkage between a glycopyranosylidene group and a 1,2-diol grouping of component glycoses, and it is known that this interlinkage is essential for their biological activities[2].

For construction of the spiro, cyclic orthoester interlinkage, we have reported[3,4] a new method by condensation of an aldonolactone and a di-*O*-trimethylsilyldiol in the presence of trimethylsilyl trifluoromethanesulfonate catalyst. Moreover, in the case of the fully *O*-benzylated methyl 2,3-*O*-(D-glucopyranosylidene)-α-D-mannopyranosides (**1**) thus obtained, it was shown[5] by X-ray analysis of the corresponding hexaacetate prepared *via* the *O*-debenzylated derivatives **5**, that the isomer that had a larger rotational value and a larger chemical shift (δ) of the orthoester carbon atom had the (*S*)-absolute configuration at that carbon atom. This paper describes the preparation of several analogs by hydrogenolysis of previously reported compounds, and their anthelmintic activity for *Ascaridia galli*.

The aforementioned result of X-ray analysis can be tentatively applied for designation of the absolute configuration to one pair of methyl 2,3-*O*-(D-glycopyranosylidene)-α-D-mannopyranoside derivatives, among which a similar interrelation of rotational value and ^{13}C-chemical shift was observed. In a way similar to that used for the conversion of **1** into **5** (ref. 5), methyl 2,3-*O*-[6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-(*R,S*)-D-glucopyranosylidene]- (**2**) (ref. 4), -[6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-(*R*)- and -(*S*)-D-galactopyranosylidene]- (**3**) (ref. 4), and 2,3-*O*-[4-azido-2,3,6-tri-*O*-benzyl-4-deoxy-(*R*)- and -(*S*)-D-galactopyranosylidene]-α-D-mannopyranoside[4] (**4**) were hydrogenolyzed into the corresponding methyl 2,3-*O*-(aminodeoxy-D-glycopyranosylidene)-α-D-mannopyranosides [(*R,S*)-**6**, (*R*)-**7**,

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**Present address: Research Laboratory of Tamura Seiyaku Co., Azusawa, Itabashiku, Tokyo 175, Japan.
†To whom correspondence should be addressed.

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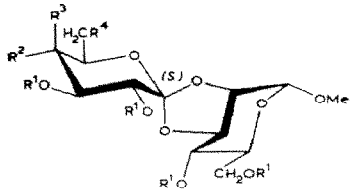
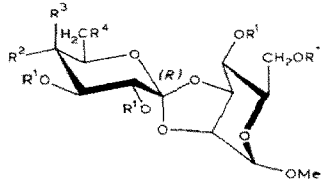
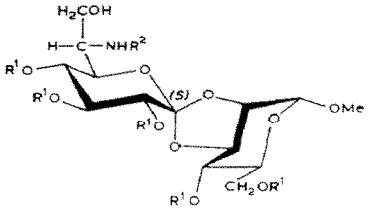
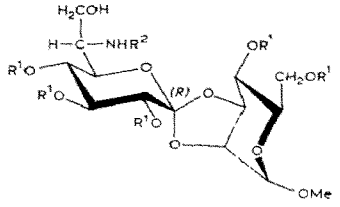


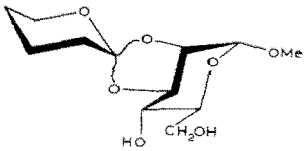


	R^1	R^2	R^3	R^4
1	Bn	OBn	H	OBn
2	Bn	OBn	H	N_3
3	Bn	H	OBn	N_3
4	Bn	H	N_3	OBn
5	H	OH	H	OH
6	H	OH	H	NH_2
7	H	H	OH	NH_2
8	H	H	NH_2	OH





9 $R^1 = Bn, R^2 = CO_2Bn$
10 $R^1 = R^2 = H$



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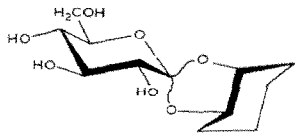

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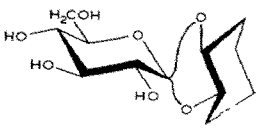

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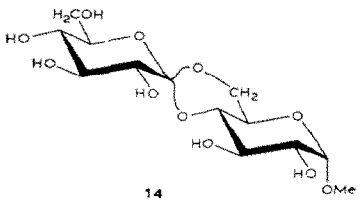

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TABLE I

PHYSICAL PROPERTIES AND ANTHELMINTIC ACTIVITY OF GLYCOPYRANOSYLIDENE ACETALS

Compound	*M.p. (degrees, dec.)*	$[\alpha]_D^{20-25}$ *(degrees; c, water)*	*Yield (%)*	*Elemental analysis (%)*[a]			*Anthelmintic rate (%)*
				C	*H*	*N*	
(*S*)-**5**	165–170	+54 (3.4)	69	44.63	6.20		60
(*R*)-**5**	160–170	+42 (2.0)	71	44.51	6.39		64
(*R,S*)-**6**	160–170	+48 (1.4)	66	44.31	6.81	3.87	81
(*S*)-**7**	160–170	+39 (2.0)	26	44.06	6.66	3.81	
(*R*)-**7**	160–170	+28 (3.0)	30	44.34	6.44	4.01	36
(*S*)-**8**	170–180	+23 (2.0)	33	44.04	6.82	4.13	100
(*R*)-**8**	165–175	+19 (1.6)	31	44.55	6.86	3.78	94
(*S*)-**10**	175–185	+8.2 (0.6)	62	44.19	6.91	3.59	100
(*R*)-**10**	180–190	+3.1 (0.8)	67	43.65	6.87	3.72	100
11a	160–165	+38 (0.4)	87	52.96	7.15		100
11b	160–165	+11 (0.5)	79	51.82	7.39		52
12a	180–190	+60 (2.2)	66	51.85	7.04		98
12b	170–180	+29 (1.6)	81	52.44	7.37		79
13a	155–165	+20 (0.6)	95	51.98	7.12		32
13b	160–170	+62 (1.0)	85	51.73	6.89		57
14	160–170	+46 (1.0)	69	43.77	6.09		54

[a] *Anal.* Calc. for $C_{13}H_{22}O_{11}$ (**5** and **14**): C, 44.07; H, 6.26; for $C_{13}H_{23}NO_{10}$ (**6, 7,** and **8**): C, 44.19; H, 6.56; N, 3.96%; for $C_{14}H_{25}NO_{11}$ (**10**): C, 43.86; H, 6.57; N, 3.65; and for $C_{12}H_{20}O_7$ (**11, 12,** and **13**): C, 52.16; H, 7.30.

(*S*)-**7**, (*R*)-**8**, and (*S*)-**8**]. Similarly the two methyl 4,6-di-*O*-benzyl-2,3-*O*-[2,3,4-tri-*O*-benzyl-6-(benzyloxycarbonyl)amino-6-deoxy-L-*glycero*-D-*gluco*-heptonopyranosylidene]-α-D-mannopyranosides[4] (**9**) were hydrogenolyzed into (*S*)-**10** and (*R*)-**10**, respectively.

On the other hand, the minor isomer [orthoester C: δ 120.3, $[\alpha]_D^{20-25}$ +46.7° (*c* 1.1, chloroform)] of methyl 4,6-di-*O*-benzyl-2,3-*O*-(oxolane-2-ylidene)-α-D-mannopyranoside[3] could be separated from the major product in the ratio of 1:8.2 (49.7%). The absolute configurations of the isomers of this pair and of those of 1,2-*O*-(2,3,4,6-tetra-*O*-benzyl-D-glucopyranosylidene)-*trans*-[6] and -*cis*-cyclohexandiols[6], though the pair is formed of (*R,S*)-isomers in the former and diastereomers in the latter, cannot be designated at the present stage.

Therefore, the isomer having the larger chemical shift of the orthoester carbon atom was designated "**a**" and the other "**b**". Hydrogenolysis of these compounds gave compounds **11a, 11b, 12a, 12b, 13a,** and **13b**, respectively. One isomer of methyl 2,3-di-*O*-benzyl-4,6-*O*-(2,3,4,6-tetra-*O*-benzyl-D-glucopyranosylidene)-α-D-glucopyranoside[6] was also hydrogenolyzed to give **14**. The physical properties of the products and their anthelmintic activities are summarized in Table I.

White Leghorn chicks of 10-day age were used for the examination of the anthelmintic activity. They were infested with 300 infective eggs of *Ascaridia galli*, and were divided into 15 groups of two each on the 35th day. Chicks were individu-

ally kept in cages, and were given a medicated feed containing 10 p.p.m. of the test compounds for 4 weeks. The total number of parasites excreted in feces during the period of medication (A) and the number of surviving worms according to intestine necropsy after treatment (B) were determined, and the "anthelmintic rate" was calculated as follows: Anthelmintic rate (%) = A/(A + B) × 100. Anthelmintic rates of the test compounds are shown as the mean values obtained from two chicks. For example, the rates of destomycin A were 100 and 100%, whereas those of (*R*)-**8** were 87 and 100%, and of **12b** 73 and 85.7%, respectively. It is interesting that all compounds were effective against *Ascaridia galli* and had not any adverse reaction on chicks. These compounds showed no insecticidal activity against *Blattella germanica* (1000 p.p.m. in aqueous sugar bait) and *Tetranychus cinnabarinus* (1000 p.p.m. in spray solution) and also no antimicrobial activity against various phytopathogens (100 p.p.m. in agar medium). It is known that destomycins[7] and hygromycin B (ref. 8), which have an additional aminocyclitol residue, show anthelmintic, as well as antimicrobial[8,9] and insecticidal[9] activities. Therefore, it seems likely that the various biological activities correspond to parts of the molecule.

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