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The Sugar Component of Aranciamycin: 2-*O*-Methyl-L-rhamnose[1]

On acid-catalyzed methanolysis, the antibiotic aranciamycin yielded the aglycone, aranciamycinone $C_{20}H_{16}O_8$, and a methylglycoside (II) of a 6-deoxyaldohexose monomethylether, which was characterized as its crystalline diacetate, mp 70–71°[2]. The derivatives of the sugar described earlier are not suitable for a detailed NMR analysis, since the signals of H–C–1 overlap with those of other protons giving a complex absorption region. Therefore the methylglycoside was hydrolyzed to the free sugar methylether (2*N* sulfuric acid, 6 h, reflux) which was directly acetylated to an oily triacetate. After chromatographic purification, the new derivative seemed to be homogeneous by thin-layer chromatography. The NMR-spectrum, however, showed signals of 2 anomeric triacetates (IV and V). Since the ratio of the components was about 4:1, most of the signals, including all the important ones, could be assigned without difficulty (Table 1).

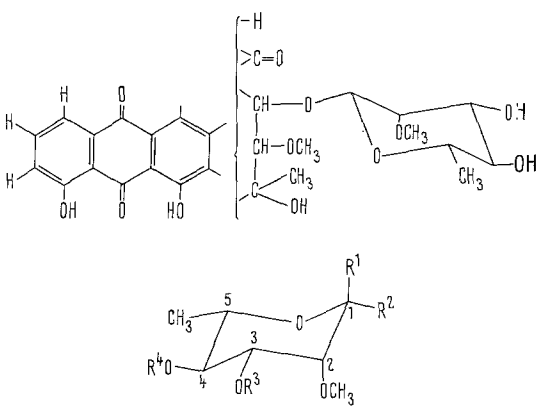
The signals of H–C–1 of both anomers at lowest field were nicely separated from other signals and were therefore advantageous as a starting point for spin decoupling experiments. These showed a coupling between the signals at δ 6.08 ppm (H–C–1 of the predominant anomer) and 3.58 ppm, which must be the signal of H–C–2. According to its chemical shift, this proton is adjacent to an ether rather than an ester oxygen atom; the sugar from aranciamycin is hence a 2-*O*-methyl-6-deoxyaldohexose.

The signal of H–C–1 of the predominant anomer (δ 6.08 ppm) is a doublet showing a coupling constant $J_{1,2} = 1.5$ Hz. In the minor component the corresponding coupling constant is even smaller, $J_{1,2} < 1$ Hz accounting for the appearance of the H–C–1 signal at δ 5.69 ppm as a broadened singlet. An axial hydrogen at C–2 would be antiperiplanar to H–C–1 of one of the anomers, causing a coupling constant of at least 8 Hz. The small coupling constants prove the equatorial position of the hydrogen atom at C–2.

Since the signals of H–C–3 and H–C–4, both adjacent to acetoxy groups, fall together at δ 5.1 ppm, no coupling is observable between them. On the other hand, a large coupling constant of about 9 Hz is recognizable within this group of signals establishing an antiperiplanar arrangement and hence an axial position for both H–C–4 and H–C–5.

The stereochemical assignment at the anomeric centres of both isomers could be made by NMR-spectroscopy. Recently SINCLAIR and SLEETER[3] have found that in 6-deoxyhexoses the CH_3-doublet of the α-glycoside is always found at somewhat higher field than that of the corresponding β-glycoside. Since the 1 ppm region in the spectrum of the triacetate mixture showed an intensive doublet (ca. 2.4 H) at 1.18 ppm and a small one at 1.22 ppm, the major component is the α-triacetate. Consequently only the relative configuration at C–3 and the absolute configuration of the sugar remain to be determined.

Of the two 2-*O*-methyl-6-deoxyhexoses with an axial *O*-methyl group at C–2 and equatorial substituents at C–4 and C–5, 2-*O*-methylrhamnose (I, L-enantiomer) is known as a synthetic compound[4]. The D-enantiomer was



	R^1	R^2	R^3	R^4
I	OH or H	H or OH	H	H
II	OCH_3	H	H	H
III	OCH_3	H	Ac	Ac
IV	OAc	H	Ac	Ac
V	H	OAc	Ac	Ac
VI	H	OCH_3	Ac	Ac

[1] 82nd communication of the series: Metabolic Products of Microorganisms. 81st comm. see: H. DIEKMANN, Arch. Mikrobiol., in press (1970).

[2] W. KELLER-SCHIERLEIN, J. SAUERBIER, U. VOGLER and H. ZÄHNER, Helv. chim. acta *53*, 779 (1970).

[3] H. B. SINCLAIR and R. T. SLEETER, Tetrahedron Lett. *1970*, 833.

[4] H. B. MACPHILLAMY and R. C. ELDERFIELD, J. Org. Chem. *4*, 150 (1939).

found to be a natural product[5]. As an intermediate of the synthesis by MACPHILLAMY and ELDERFIELD[4], the methylglycoside diacetate (III or IV or a mixture of both) was prepared also; unfortunately this derivative was not purified and characterized. We repeated the synthesis, starting from authentic L-rhamnose, and isolated the methyl glycoside diacetate by chromatography on silica gel. The semi-solid product showed a single spot on thin-layer chromatography but the NMR-spectrum showed the presence of 2 anomeric glycosides in a ratio of about 3:1, the predominant component being different from the degradation product, mp 70–71°, of aranciamycin. By crystallization, a single compound of mp 112–113° and $[\alpha]_D = +77°$ (in methanol) was obtained. This proved later to be the β-glycoside VI (see below).

Table I. NMR-spectrum of the mixture of α- and β-1,3,4-tri-*O*-acetyl-2-*O*-methylrhamnose (4:1), $CDCl_3$, 100 MHz

δ	Splitting	J	Integral	Assignments
1.18	d	6 Hz	ca. 2.4 H	CH_3 of α-anomer
1.22	d	6	ca. 0.6 H	CH_3 of β-anomer
2.00	s		3 H	3 OAc (both anomers)
2.04	s		3 H	
2.10	s		3 H	
3.45	s		ca. 2.4 H	OCH_3 (α)
3.54	s		ca. 0.6 H	OCH_3 (β)
3.58	t	1.5	ca. 0.8 H	H–C–2 (α)
ca. 3.85	m		ca. 1 H	H–C–5 (both anomers)
ca. 5.1	complex		2 H	H–C–3, H–C–4 (both an.)
5.69	s		ca. 0.2 H	H–C–1 (β)
6.08	d	1.5	ca. 0.8 H	H–C–1 (α)

Table II. NMR-spectra of the anomeric methylglycoside diacetates of 2-*O*-methyl-L-rhmnose, $CDCl_3$, 100 MHz

β-Anomer (mp 112°)			α-Anomer (mp 70°)			
δ	Splitting	Integral	δ	Splitting	Integral	Assignments
1.24	d, 6 Hz	3 H	1.20	d, 6 Hz	3 H	CH_3–6
2.00	s	3 H	2.02	s	3 H	OAc
2.05	s	3 H	2.05	s	3 H	OAc
3.53	s	3 H	3.40	s	3 H	OCH_3
3.56	s	3 H	3.48	s	3 H	OCH_3
3.2–3.6	m	1 H	ca. 3.8	m	1 H	H–C–5
3.70	d, 2.5 Hz	1 H	3.64	t, 1.5 Hz	1 H	H–C–2
4.41	s	1 H	4.73	d, 1.5 Hz	1 H	H–C–1
4.7–5.3	complex	2 H	510–5.3	complex	2 H	H–C–3 and H–C–4

The mother liquors, a mixture of both anomers, were epimerized (*p*-toluenesulfonic acid in methanol, 4 h, reflux) and reacetylated to an oily product which was the almost pure α-glycoside diacetate III. After chromatographic purification and crystallization from petroleum ether, colorless prisms of mp 69° were obtained whose Rf value, NMR- and IR-spectra were identical with those of the degradation product of aranciamycin[2]. Since the synthetic as well as the natural derivative show $[\alpha]_D = -69°$ (methanol), the sugar component of aranciamycin is 2-*O*-methyl-L-rhamnose (I).

The assignments of the anomeric configurations of the two crystalline methylglycoside diacetates again follow from SINCLAIR's and SLEETER's rule[3] (see above). The derivative of mp 112° shows the CH_3 doublet at lower field (Table II) and is therefore the β-glycoside VI while the anomer of mp 70° is the α-glycoside III. This assignment is confirmed by the optical rotations. According to HUDSON's rule[6], the L-α-glycoside (mp 70°) is levorotatory and the L-β-glycoside (mp 112°) is dextrorotatory.

In aranciamycin itself the signal of H–C–1 of the sugar moiety occurs at δ 5.49 ppm (KELLER-SCHIERLEIN et al.[2], Figure 3) as a singlet. This corresponds to the singlet signals of H–C–1 in the β-triacetate V (Table I) and the β-methylglycoside diacetate VI (Table II). Aranciamycin is therefore a β-2-*O*-methyl-L-rhamnoside of aranciamycinone. Since aranciamycin shows 2 secondary (acetylable) alcoholic hydroxyl groups, while aranciamycinone contains 1 such group[2], the secondary hydroxyl of the aglycone is involved in the glycosidic linkage of the antibiotic. The partial structure of the aglycone[2] given earlier can be extended to the partial formula VII for aranciamycin[7].

Zusammenfassung. Der Zuckerbaustein des Antibiotikums Aranciamycin ist die 2-*O*-Methyl-L-rhamnose.

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[6] C. S. HUDSON, J. Am. chem. Soc. *47*, 268 (1925).

[7] We are grateful to Prof. H. ZÄHNER, Tübingen, for aranciamycin, and to CIBA Ltd., Basle, for financial support.

Heartwood Constituents of *Pinus formosana*

The formosan pine, *Pinus formosana* Hayata, grows in the mountains of Taiwan and morphologically is considered a variety of the Japanese white pine, *P. parviflora* Sieb. and Zucc. This species has been placed in the group Strobi, subgenus Haploxylon[1]. It will be recalled that the Haploxylon pines contain both flavones and flavanones, as well as stilbene derivatives, while the Diploxylon pines possess only stilbenes and flavones. Generally, pines belonging to these two subgenera can be distinguished by their specific content of heartwood phenolics[2–5]. Since any deviations from a general pattern are of interest in phytochemical work, it was decided to make a brief investigation of this tree.

A benzene extract of the heartwood was treated with sodium hydroxide solution. The aqueous layer was removed, then acidified to precipitate a semi-crystalline oil. Chromatography over silicic acid gave dehydroabietic and isopimaric acids, plus pinostrobin and tectochrysin.