die spez. Drehung, $[\alpha]_D$ −24,6° in Chlf., entgegengesetzt gleich. Durch Solvolyse mit Natriummethylat (siehe oben) wurde freie L-Lyxose erhalten und durch Papierchromatographie identifiziert. L-Lyxose wurde auch als Baustein von Curamycin nachgewiesen[8].

Aus den nachgewiesenen Abbauprodukten geht klar hervor, dass die Antibiotica Curamycin und Avilamycin nahe miteinander verwandt sind. Worin der eindeutig feststellbare Unterschied besteht, konnte dagegen bisher nicht abgeklärt werden. Die aus Avilamycin erhaltenen Bruchstücke enthalten zusammen 38 C-Atome. Es sind demnach entweder grössere Bausteine mit insgesamt ca. 25 C-Atomen bisher nicht aufgefunden worden, oder einzelne Zucker sind in der Avilamycinmolekel mehrfach vorhanden. Der Unterschied zwischen Avilamycin und Curamycin liegt daher entweder darin, dass sich weitere vorhandene Bausteine dem Nachweis entzogen haben oder aber, dass die Anzahl oder Anordnung der nachgewiesenen Bausteine darin verschieden sind.

Das Antibioticum Avilamycin besitzt eine hohe Wirkung gegen grampositive Bakterien in vitro und zeigt am Versuchstier eine chemotherapeutische Wirkung bei s.c. Verabreichung[10].

Kürzlich ist über die Isolierung von 2 neuen Antibiotica, den Everninomycinen B und D, berichtet worden[11–13], die als aromatischen Baustein ebenfalls die Dichlor-isoeverninsäure enthalten. Die Struktur der Zuckerbausteine der Everninomycine wurde nicht vollständig aufgeklärt. Der mit dem Acylrest direkt verbundene Zucker ist jedoch verschieden von der 2-Desoxy-rhamnose, und die Everninomycine enthalten im Gegensatz zu Avilamycin, Curamycin und wahrscheinlich Exfoliatin je einen Aminozucker-Rest.

Summary. A strain of *Streptomyces viridochromogenes* produced a new crystalline antibiotic, Avilamycin, related to but not identical with Curamycin and Exfoliatin. Avilamycin, $C_{63}H_{94}O_{35}Cl_2$, gave on solvolytic degradation the following products: dichloroisoeverninic acid, 2-deoxy-D-rhamnose, 2,6-di-*O*-methylmannose, 4-*O*-methylfucose, L-lyxose and 3,5-diacetoxy-γ-caprolactone.

F. Buzzetti, F. Eisenberg, H. N. Grant, W. Keller-Schierlein, W. Voser und H. Zähner[14]

Organisch-chemisches Laboratorium und Institut für spez. Botanik der Eidg. Technischen Hochschule, Zürich, und Forschungslaboratorien der Ciba Aktiengesellschaft, Basel (Schweiz), 12. Januar 1968.

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Curamycin. II. Structure of the Hydrolysis Products 'Curacin' and 'D-Curamicose'

Galmarini and Deulofeu[1] reported that curamycin, m.p. 198°, $[\alpha]_D$ − 5.3° ($CHCl_3$), a chlorine containing antibiotic isolated from cultures of *Streptomyces curacoi*, produced on acid hydrolysis a crystalline product which was named curacin, and a mixture of monosaccharides. Curacin, which contained all the chlorine atoms present in the antibiotic, was found to be the ester of dichloroisoeverninic acid with a dideoxyaldose whose structure was not established. The mixture of sugars was shown to be formed by 3 monosaccharides, 2 of which were identified as L-lyxose and 4-*O*-methyl-D-fucose, the structure of the latter being confirmed by synthesis[2]. The structure of the third component which was named 'sugar 1' from its chromatographic behaviour was not determined at that time.

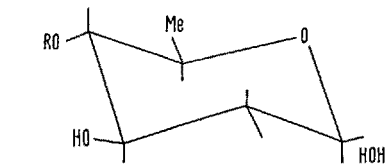
After our publication we were kindly informed by Prof. V. Prelog and Dr. W. Keller-Schierlein of their work on an antibiotic named avilamycin[3] which was very similar although not identical with curamycin. On acid hydrolysis it also produced curacin and several other products, among them 3 monosaccharides which were found to be chromatographically identical to those obtained from curamycin. Prof. Prelog and Dr. Keller-Schierlein also determined that the dideoxyhexose present in curacin behaved on paper chromatography as the 2,6-dideoxy-L-*arabino*-hexose.

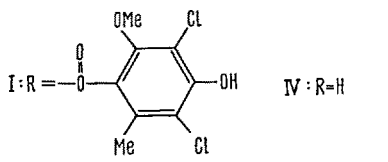
From the above mentioned investigators we received a generous sample of avilamycin and of several of its hydrolysis products which permitted a full determination of the structure of curacin and the identification of the third monosaccharide, D-curamicose (earlier named sugar 1), as the hitherto unknown 2,6-di-*O*-methyl-D-mannose (V).

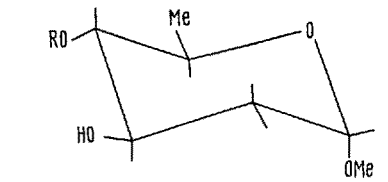
When curacin (1) (from curamycin and avilamycin) was boiled with methanol containing hydrogen chloride (10 mg/ml), a crystalline compound, the methyl glycoside of curacin (II) was readily obtained, m.p. 148–150°, $[\alpha]_D^{24}$ + 54.5° ($CHCl_3$). This methyl glycoside when treated with 1*N* sodium hydroxyde at 100° yielded dichloroisoeverninic acid and the methyl glycoside of the dideoxyhexose (III) present in curacin. It failed to crystallize and was hydrolyzed at room temperature with 0.5*N* sulphuric acid. The free sugar was purified by distillation and could be crystallized, m.p. 85–91°, $[\alpha]_D^{24}$ + 28.8 (10 min) → + 13.2° (final, H_2O). It was identified as the 2,6-dideoxy-D-*arabino*-hexose (IV), a sugar already found in several natural products[4–6] and whose structure has been fully confirmed by synthesis[7]. IR- and NMR-spectra were in agreement with its structure.

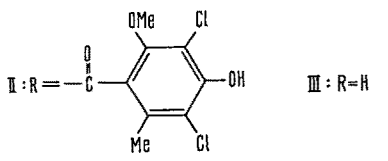
When the NMR-spectra of the methyl 2,6-dideoxy-D-*arabino*-hexoside[4] and of the methyl glycoside of curacin (II) are compared, it is clearly seen that the dichloro-

isoeverninyl residue esterifies the hydroxyl group at C-4 of the 2,6-dideoxy-D-*arabino*-hexose. The relevant signals in the NMR-spectrum of the methyl glycoside of curacin are ($CDCl_3$, δ units and J in cps): 1.26 (d; J = 6; C-methyl); 3.34 (s; glycosidic *O*-methyl); 4.80 (t; J = 2; equatorial C_1-H); 4.86 (t; J = 9; C_4-H, 2 axial-axial couplings). For the methyl glycoside of 2,6-dideoxy-D-*arabino*-hexose the corresponding signals (in D_2O) are: 1.25 (d; J = 6; C-methyl); 3.33 (s; *O*-methyl); ca. 4.80 (C_1-H, almost covered by the HDO signal); 3.08 (t; J = 9; C_4-H), the diamagnetic shift of the C_4-H clearly shows that the dichloroisoeverninyl residue had been located at that carbon atom; 1.83 and 2.09 (double quartet; $J_{gem} = 14$, $J_{H_{2a}-H_3} = 6$, $J_{H_{2e}-H_3} = 4$).



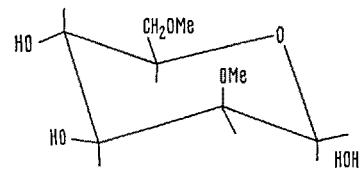






The NMR-spectrum of curacin (acetone-d_6) confirmed the former conclusions about the position of the ester group and also showed that while the methyl glycoside of curacin is a pure α-anomer, curacin appears, in the solvent employed, as a mixture of both anomers; δ 1.26 (d; J = 6 cps; C-methyl); 1.68 and 2.10 (m; C_2-methylene); 4.74 (q; $J_{aa} = 9.5$, $J_{ae} = 2.5$; C_1-H axial); 4.98 (broad signal; C_4-H); 5.32 (q; $J_{ae} = 3$, $J_{ee} = 1.5$; C_1-H equatorial). For the above reasons the conformation of the hexose moiety in curacin is the same as in the methyl 2,6-dideoxy-D-*arabino*-hexoside, hence the dichloroisoeverninyl residue is equatorial and not a factor of conformational instability. This structure for curacin is also in agreement with the lack of consumption of periodate on oxidation.

The identification of D-curamicose as 2,6-di-*O*-methyl-D-mannose (V) was done by purification of the sugar by repeated high vacuum distillation when a glassy product $[\alpha]_D^{20} + 10.3°$ (H_2O) was obtained, whose NMR-spectrum showed the presence of 2 *O*-methyl groups (δ 3.38 and 3.46) and of an hemiacetalic proton (δ 5.23; d; J = 1.5 cps). Demethylation of the sugar with boron-trichloride[8] yielded a product which was identified as D-mannose by paper chromatography, electrophoresis and preparation of the *p*-nitroanilide[9]. The sugar gave, upon treatment with phenylhydrazine, a phenylosazone, m.p. 183–184°, $[\alpha]_D^{20} - 76.6$ (10 min) $\rightarrow -43.7°$ (final, absolute ethanol) which was found to be identical to 6-*O*-methyl-D-glucose phenylosazone[10]. As the other *O*-methyl group was eliminated during osazone formation, it is evident that it was placed on carbon atom 2 and accordingly the original sugar is 2,6-di-*O*-methyl-D-mannose. Correct analyses were obtained for all new compounds. A full account of the experiences will be published elsewhere[11].



V

Zusammenfassung. Curacin, die chlorhaltige Fraktion der milden Hydrolyse des Antibiotikums Curamycin, wurde durch ihre chemischen und physikalischen Eigenschaften als 4-*O*-Dichlor-*iso*-everninyl-2-deoxy-D-rhamnose aufgeklärt. Ausser L-Lyxose und 4-*O*-Methyl-D-fucose besitzt auch das Curamycin ein drittes Monosaccharid, D-Curamicose, welches als 2,6-Di-*O*-methyl-D-mannose identifiziert wurde.

E. G. GROS, V. DEULOFEU,
O. L. GALMARINI and B. FRYDMAN

Departamento de Química Orgánica, Facultad de Ciencias Exactas y Naturales, Facultad de Ingeniería and Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires (Argentina), 12 January 1968.

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