THE STRUCTURE OF AKLAVIN

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The antibiotic aklavin was isolated in 1956 from culture liquids of an unknown streptomycete obtained from soil samples originating in Aklavik, Canada[1]. It showed activity against various bacteriophages, gram-positive bacteria, and some fungi and viruses. Following preliminary characterization, it was subjected to acid hydrolysis, which cleaved it into an aglycone and a basic sugar or sugars. The structure of this aglycone, aklavinone, was shown to be 1-deoxy-ε-pyrromycinone[2]. However, the sugar moiety never was identified.

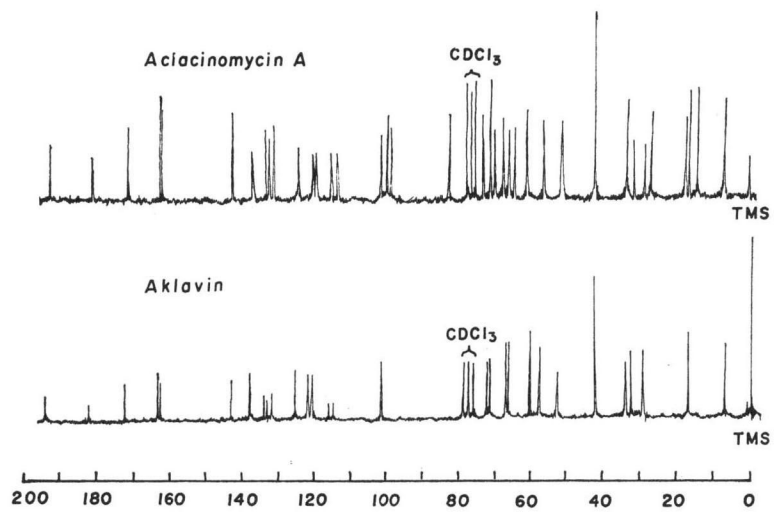
More recently the discovery and structure elucidation of the antibiotic aclacinomycin (**II**) was reported[3]. Although this antibiotic contains the same aglycone as aklavin, it has much superior antibacterial and antitumor activity. Since this difference in biological activity obviously resides in the sugar portion of the two molecules, it seemed worthwhile to elucidate the sugar or sugars present in aklavin for the purpose of defining structure-activity relationships.

Samples of aklavin hydrochloride (NSC 100290) supplied by Dr. ULRICH WEISS of the National Institutes of Health were purified by recrystallization from acetone-petroleum ether. Comparison of the ^{13}C nmr spectra of aklavin free base and aclacinomycin A, obtained from the Sanraku-Ocean Company, Ltd., in deuteriochloroform (Fig. 1) revealed that aklavin had peaks identical to those of the aglycone and rhodosamine parts of aclacinomycin A, but aklavin lacked the two additional sugars, 2-deoxyfucose and cinerulose, present in aclacinomycin A. The chemical shifts of the aklavin peaks are assigned in Table 1. These assignments are based, in part, on standard chemical shift calculations. In addition, the model compounds ε-rhodomycinone and pyrromycin were used, along with ^{1}H off-resonance and ^{1}H single frequency decoupling experiments. A more rigorous treatment would be necessary to absolutely assign all the carbon atoms, hence several of the assignments may be reversed and are so indicated below.

The ^{13}C nmr spectra were recorded on a Varian XL-100 NMR Spectrometer operating at 25.2 MHz in the FT mode. $CDCl_3$ was used as the solvent and as the deuterium signal for the field-frequency lock channel. Chemical shifts were measured against internal TMS.

Thus it appeared that aklavin was identical with 1-deoxypyrromycin (**I**), which already had been reported as a product of the partial hydrolysis of

Fig. 1. ^{13}C nmr spectra of aklavin and aclacinomycin



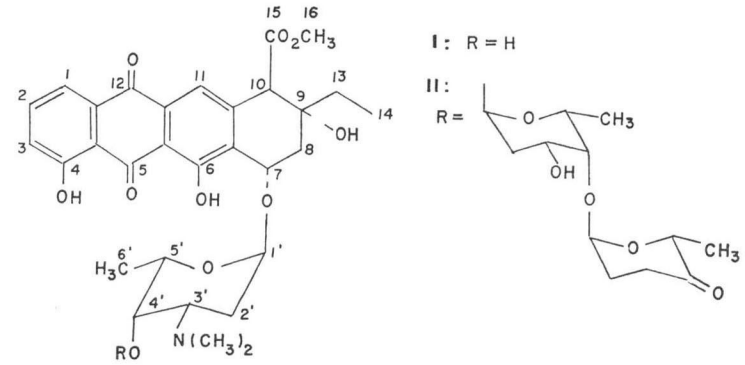


Table 1. ^{13}C nmr chemical shifts of aklavin in $CDCl_3$

Chemical shift ppm	Assignment C-no.	Chemical shift continued	Assignment C-no.
6.67	14	114.48	4a
17.00	6′	115.60	5a
28.82	13	119.97	1
32.09	2′	120.76	11
33.66	8	124.59	3
41.93	$N(CH_3)_2$	131.17	11a
52.43	16	132.69	6a
57.09	10	133.27	12a
59.51	3′	137.14	2
65.86	7	142.47	10a
66.36	5′	161.92	4
70.99	4′	162.32	6
71.65	9	171.02	15
101.31	1′	180.97	12
		192.39	5

aclacinomycin[3]. We repeated this partial hydrolysis under the specified conditions, but found them too vigorous. Better yields of 1-deoxypyrromycin were obtained by treating a methylene chloride solution of aclacinomycin (6 mg in 4 ml) with 2~3 drops of 1% methanolic hydrogen chloride. The reaction was complete at 25°C in 10 minutes. The sample prepared in this manner had Rf values identical with those of aklavin in two different solvent systems: chloroform - methanol (4 : 1) and ethyl acetate - methanol (3 : 7) on silica gel plates. A hydrolysis sample purified by chromatography in the former system had an infrared absorption spectrum superimposable with that of aklavin hydrochloride.

Acknowledgements

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References

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