Structure of the Polyether Antibiotic K-41 by Mass and Nuclear Magnetic Resonance Spectrometry

By JOHN L. OCCOLOWITZ,* DOUGLAS E. DORMAN, and ROBERT L. HAMILL
(*Lilly Research Laboratories, Division of Eli Lilly and Company, Indianapolis, Indiana* 46206)

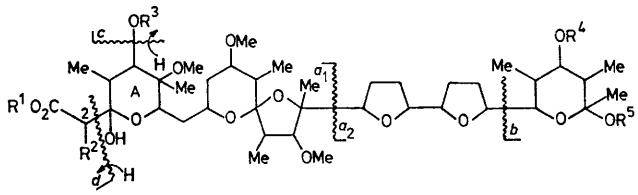
Summary Using electron impact and field desorption mass spectrometry and n.m.r. spectrometry, the polyether antibiotic K-41 has been assigned structure (**1**).

THE accompanying communication[1] describes determination of the structure of the antibiotic K-41[2] using *X*-ray diffraction. By personal communication, we found that A32887, an antibiotic produced at these laboratories by *Streptomyces albus* NRRL 11109, was identical to K-41. We outline here independent and concurrent work leading to our proposal of the structure (**1**) for K-41 (A32887).

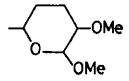
The molecular formula $C_{48}H_{82}O_{18}$ for (**1**) was established by accurate mass measurement of the molecular ion (M^+)† in its field desorption (F.D.) spectrum and by microanalysis. A similar formula, $C_{49}H_{84}O_{17}$, for A204A (**2**), a polyether antibiotic of known structure,[3] prompted us to compare the n.m.r. and mass spectra of these two compounds in detail.

The ^{13}C- and ^1H-n.m.r. spectra of the sodium salt of (**1**) are similar to the spectra of the sodium salt of (**2**). In particular, the n.m.r. spectra indicate the presence of the sugar unit and the spiroacetal system in (**1**). However, the quartet in the ^1H spectrum[4] of the sodium salt of (**2**) due to the hydrogen

† Two formulae, $C_{48}H_{82}O_{18}Na$ and $C_{55}H_{78}O_{13}Na$, give peaks within the range 969·5373 ± 0·010 found by peak matching with a field ionized reference standard of hexakis-(2,2,3,3-tetrafluoro-propoxy)cyclotriphosphazene at resolution 8000. The latter formula was excluded by microanalysis.



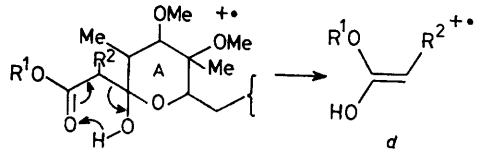
in (1)–(10), 'sugar' =



	R^1	R^2	R^3	R^4	R^5	
(1)	H	OH	Me	Sugar	H	(K-41)
(2)	H	Me	Sugar	Me	H	(A204A)
(3)	Me	Me	Sugar	Me	H	
(4)	Me	OH	Me	Sugar	H	
(5)	H	OAc	Me	Sugar	H	
(6)	Ph_2CH	OH	Me	Sugar	Me	
(7)	Me	OCOPh	Me	Sugar	Me	
(8)	Me	OH	Me	Sugar	Me	
(9)	Me	OH	Me	Sugar	CD_3	
(10)	Me	Me	Sugar	Me	Me	

at C-2 is missing in the ^1H spectrum of the sodium salt of (**1**). A prominent peak at *m/e* 129 ($C_7H_{13}O_2$) in the electron impact (E.I.) and F.D. spectra of (**1**) and (**2**) supports the presence of the sugar unit in (**1**).

The E.I. and F.D. spectra of the methyl ester (**3**) of A204A(**2**) show a prominent peak a_1 at *m/e* 645. In the E.I. spectrum, a_1 fragments by elimination of the molecules *c* and *d* to give the ion $C_{22}H_{35}O_7$ which further fragments by the successive elimination of three molecules of methanol. The E.I. and F.D. spectra of the methyl ester (**4**) of K-41 (**1**) show no *m/e* 645 peak but instead a peak at *m/e* 533. In the E.I. spectrum, an ion $C_{23}H_{39}O_8$ fragments by the successive elimination of 4 molecules of methanol. All the foregoing data can be accommodated by having R^2 = OH and R^3 = Me in the structure of (**1**); the elemental composition of *m/e* 533 (a_1) supports this conclusion. Formation of an acetate (**5**) by (**1**) but not by (**2**) indicates the presence of an additional hydroxy in (**1**).

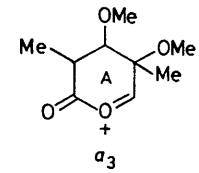


SCHEME

(**6**) *m/e* 242, $C_{15}H_{14}O_3$
(**7**) *m/e* 194, $C_{10}H_{10}O_4$

Definitive evidence for the presence of the unit CO_2H–CH(OH)– in (**1**) comes from the E.I. spectra of its diphenylmethyl ester methyl ether (**6**) and methyl ester methyl ether benzoate (**7**). The E.I. spectra of both (**6**) and (**7**) show the fragmentation in the Scheme. That the itinerant hydrogen involved in the McLafferty rearrangement is an exchangeable one is shown by a **1** a.m.u. shift to higher mass of the ions *d* when the E.I. spectra of (**6**) and (**7**) exchanged with CH_3OD are determined. The presence of the hydroxy-group α to the carboxylic acid group of (**1**) results in its pK_a being two units lower than the pK_a of (**2**).

The E.I. spectra of (**1**) or its derivatives yield no discernible evidence regarding the units a_2 or *b*. However, the F.D. spectrum of the methyl ester methyl ether (**8**) of (**1**), taken somewhat above the best anode temperature, yields the peaks a_2 and *b* having the correct elemental composition. In the F.D. spectrum of the methyl ester deuteriomethyl ether (**9**) of (**1**) the peaks a_2 and *b* are shifted 3 a.m.u. to higher mass. Analogous fragments were observed in the F.D. spectrum of the methyl ester methyl ether (**10**) of (**2**).



a_3

A fragment $C_9H_{15}O_4^+$ to which we assign the structure a_3 occurs in the E.I. spectra of compounds (**7**) and (**9**). It arises from fragment a_1, without molecule *d* and two molecules of methanol, and most likely represents ring (A) rather than another portion of (**1**).

Although the foregoing data do not result in a rigorous structure determination of such a relatively complex molecule as (**1**), they were sufficient, taken in conjunction with the knowledge of the structures of similar compounds, to lead to a correct structure proposal. The application of these methods to the structure determination of metabolites of polyethers of this type is obvious.

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