THE STRUCTURE OF AFRAGILIMYCIN A

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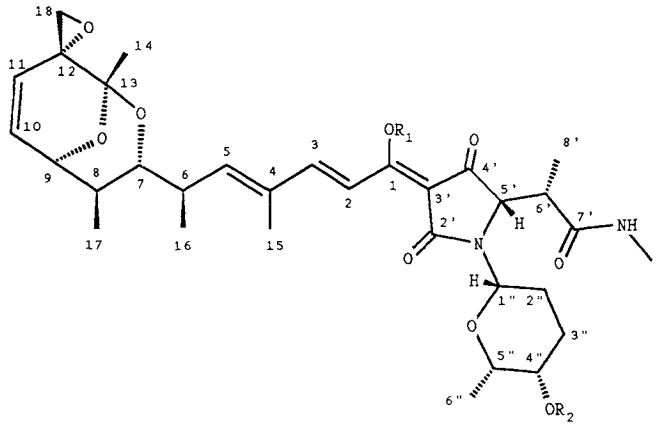
This paper describes identification of afragilimycin A (**1**) with a salt of streptolydigin.

In our search for antibiotic substances from microorganisms, we isolated afragilimycin A from a *Streptomyces* sp. Afragilimycin A, described by ARAI[1], does inhibit the growth of both Gram-positive and Gram-negative bacteria, and has intermediate toxicity. Though several physical characteristics of the compound such as IR, UV and ^{1}H NMR spectra are known, the structure of afragilimycin A has not been elucidated. ARAI has

Fig. 1. Structure of afragilimycin A (**1**), streptolydigin (**2**) and afragilimycin diacetate (**3**).



1 $R_1 = -$ $R_2 = H$
2 $R_1 = R_2 = H$
3 $R_1 = R_2 = CH_3CO$

Table 1. NMR data for afragilimycin (**1**) and its diacetate (**3**).

	^{13}C NMR chemical shift (ppm)			^{13}C NMR chemical shift (ppm)			^{1}H NMR chemical shift (ppm)			^{1}H NMR chemical shift (ppm)	
	1	**3**		**1**	**3**		**1**	**3**		**1**	**3**
C-1	185.0	185.2	C-2′	172.2	171.2	2-H	7.63 d	7.65 d	1″-H	5.56 d	5.70 d
C-2	122.9	122.7	C-3′	103.4	103.1	3-H	7.38 d	7.50 d	2″-Ha	2.11 m	1.95 m
C-3	146.8	147.1	C-4′	196.5	195.9	5-H	6.00 d	6.04 d	2″-Hb	2.06 m	1.95 m
C-4	134.4	134.2	C-5′	61.6	61.6	6-H	2.75 m	2.75 m	3″-Ha	1.39 m	1.51 m
C-5	141.0	141.2	C-6′	42.3	42.0	7-H	3.56 br s	3.61 d	3″-Hb	1.22 m	1.20 m
C-6	33.9	33.8	C-7′	174.8	173.3	8-H	1.96 m	1.95 m	4″-H	3.64 d	4.86 s
C-7	75.8	76.3	C-8′	12.6	13.1	9-H	4.35 s	4.34 t	5″-H	3.81 d	3.95 d
C-8	35.3	35.0	C-1″	79.1	78.2	10-H	6.38 dd	6.35 dd	6″-H	1.22 m	1.20 m
C-9	71.8	71.5	C-2″	30.9	28.1	11-H	5.62 d	5.61 d	NH	7.70 br s	7.60 m
C-10	134.3	134.2	C-3″	22.3	23.0	14-H	1.22 m	1.20 m	NMe	2.69 d	2.64 d
C-11	130.5	130.5	C-4″	66.1	68.1	15-H	1.86 s	1.86 s	Ac	—	2.12 s
C-12	55.4	55.1	C-5″	76.5	73.9	16-H	1.01 d	1.01 d	Ac	—	2.07 s
C-13	99.0	98.8	C-6″	17.2	17.2	17-H	0.70 d	0.68 d			
C-14	22.5	22.3	NMe	26.2	26.3	18-Ha	3.00 d	2.97 d			
C-15	12.6	12.5	1-Ac	—	170.4	18-Hb	2.83 d	2.89 d			
C-16	17.3	17.2		—	21.0	5′-H	4.05 s	3.87 s			
C-17	12.6	12.5	4″-Ac	—	170.4	6′-H	3.37 br s	3.25 d			
C-18	50.8	50.6		—	21.0	8′-H	1.39 m	1.51 m			

As solvents $CDCl_3$-CD_3OD (6:1) was used for **1** and $CDCl_3$ for **3**.

however communicated on the possible identity of afragilimycin A with streptolydigin (**2**)[2]. Streptolydigin is a well known antibiotic, that is isolated from *Streptomyces lydicus*[3,4], and ^{13}C NMR data is available on this compound[5]. As the IR spectrum, optical rotation and mp of afragilimycin A differs from those of streptolydigin (mp: 188°C (dec), (literature[1] mp: 190~195°C (dec), **2**[3,4]: MP 144~150°C); $[\alpha]_D^{20}$ −35.5° (*c* 0.12, MeOH), (literature[1] $[\alpha]_D^{20}$ −34.4° (*c* 0.12, MeOH), **2**[3,4]: $[\alpha]_D^{20}$ −64.7° (*c* 2)), we decided to study the structure using NMR.

The ^{13}C NMR spectrum of **1** revealed that the C-6~C-18 portion and the sugar moiety were identical with **2**[5]. Also C-5′~C-7′ were identical, but the 8′-methyl group at 10.3 ppm in **2** was absent. The carbons of C-1~C-5 and C-2′~C-4′ area had chemical shifts quite similar to those of the sodium salt of tirandalydigin[6], indicating the enol moiety was a salt. When DCl was added to the NMR-tube, degradation of the labile epoxide moiety occurred to a main product that contained carbons at 150.4, 146.2 and 115.5 ppm consistant with C-3, C-5 and C-2 in streptolydigin (**2**).

Acetylation of afragilimycin A with acetic anhydride in pyridine gave the diacetate **3** seen by the appearance of two acetyl groups in ^1H NMR spectrum. **3** gave better spectra than **1** due to the absence of a tautomeric equilibrium. Thus we were able to obtain a complete ^{13}C-^1H correlation of **3**, and when combined with the COSY-spectrum the entire ^1H NMR spectrum could be assigned. This showed that the 8′-methyl group was present in the multiplet at 1.51 ppm correlating to a carbon at 13.1 ppm and coupling with a proton at 3.25 ppm correlating with a carbon at 42.0 ppm assigned by comparison to **2** to be C-6′. In all other respects the ^1H and ^{13}C NMR spectra of **3** fits the assigned structure.

As the carbon resonances of all stereogenic centers in **1** and **3** are almost identical with the resonances in **2**, we concluded that the relative stereochemistry of **1** and **2** are the same.

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