STRUCTURES OF PLURAMYCIN A AND NEOPLURAMYCIN

Sir:

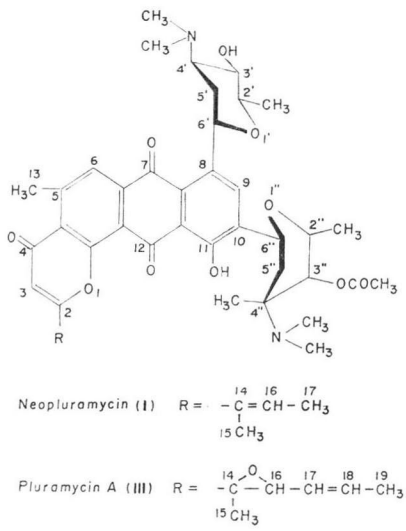
Pluramycin A[1,2] and neopluramycin[3] are potential antitumor antibiotics produced by *Streptomyces pluricolorescens* OKAMI *et* UMEZAWA and by another strain (No. MB760-MG1) of *Streptomyces pluricolorescens,* respectively. In this communication, the structural elucidation and ^{13}C chemical shift assignments for the two antibiotics are reported.

The formula $C_{41}H_{50}N_2O_{10}$ was assigned to neopluramycin (**I**) by the elemental analysis[3] and ^{13}C NMR spectrum. Acetylation of **I** with acetic anhydride in pyridine at room temperature for 24 hours afforded diacetylneopluramycin (**II**), mp 211~212°C (dec.), *m/e* 814 (M^+ for $C_{45}H_{54}N_2O_{12}$). It was identified with triacetylkidamycin[4] which was kindly supplied by Dr. I. UMEZAWA, Kitasato Institute, in all respects including the conformations of two tetrahydropyran rings. From these results, **I** is suggested to be a monoacetyl derivative of kidamycin. The structures of kidamycin and triacetylkidamycin were elucidated on the basis of the X-ray crystallographic analysis of triacetylmethoxykidamycin bis(methylammonium iodide) by FURUKAWA *et al.*[4] In ^1H NMR spectrum of **I** (Table 1), an acetyl signal is observed at δ 2.19 and the chemical shift which can be assigned to the 3″-H (δ 5.14) moves to a lower field than that of kidamycin

Table 1. Chemical shifts of ^1H NMR spectra

Proton	ppm (*J* Hz)			
	I	**II**	**III**	**IV**
2′-H	3.53 m (6, 8.5)	3.65 m (6, 9)	3.56 m (6, 9)	3.65 m (6, 9)
2′-CH_3	1.46 d (6)	1.31 d (6)	1.46 d (6)	1.32 d (6)
3′-H	3.26 dd (9, 8.5)	4.88 t (9)	3.26 t (9)	4.88 dd (9, 10)
3′-OH		—	3.15	—
3′-OAc	—	2.14 s	—	2.14 s
4′-H	2.86 m (9)	3.09 m (9)	2.87 m (9, 9)	3.11 m (10)
5′-H_{ax}	1.33 m (10)	~1.3	1.39 m (10, 9)	~1.3
5′-H_{eq}		~1.6	~1.6	~1.6
6′-H	5.39 dd (10)	5.40 dd (10)	5.43 d (10)	5.42 dd (10)
2″-H	4.31 m (7, 4.5)	4.32 m (7, 4.5)	4.32 m (7, 4.5)	4.32 m (7, 4.5)
2″-CH_3	1.51 d (7)	1.43 d (7)	1.53 d (7)	1.42 d (7)
3″-H	5.14 d (4.5)	5.20 d (4.5)	5.14 d (4.5)	5.21 d (4.5)
3″-OAc	2.19 s	2.18 s	2.20 s	2.20 s
4″-CH_3	0.93 s	0.98 s	0.93 s	1.00 s
5″-H_{ax}	1.80 dd (8.5, 14)	~1.6 dd (9.5, 14)	1.79 dd (8.5, 14)	~1.7
5″-H_{eq}	2.43 dd (4, 14)	~2.4	2.46 dd (4, 14)	~2.5
6″-H	5.54 dd (8.5, 4)	5.30 m (9.5)	5.54 dd (8.5, 4)	5.30 m (9, 4)
$N(CH_3)_2$	2.34 s	2.27 s	2.33 s	2.28 s
$N(CH_3)_2$	2.34 s	2.32 s	2.35 s	2.32 s
3-H	6.34 s	6.33 s	6.50 s	6.44 s
13CH_3	2.96 s	2.97 s	3.00 s	2.97 s
6-H	7.91 s	7.81 s	7.99 s	7.85 s
9-H	8.26 s	8.32 s	8.27 s	8.31 s
11-OH		—	13.92 bs	—
11-OAc	—	2.51 s	—	2.46 s
15CH_3	1.97 s	1.99 s	1.83 s	1.77 s
16-H	7.43 m	7.31 m (6.5)	4.15 d (8)	3.97 d (8)
17CH_3	2.01 d (7)	1.98 d (6.5)	—	—
17-H	—	—	5.40 m (11, 8, 2)	5.36 m (11, 8, 2)
18-H	—	—	6.05 m (11, 7)	6.02 m (11, 7)
19CH_3	—	—	1.88 dd (7, 2)	1.87 dd (7, 2)

Spectra were measured in $CDCl_3$ using TMS as the internal reference.



(lit.[4] δ 3.37). It indicates that the structure of neopluramycin is 3″-O-acetylkidamycin as shown by structure **I**.

The formula ($C_{43}H_{52}N_2O_{11}$) of pluramycin A (**III**) was derived from the mass spectrum (M^+, *m/e* 772). Acetylation of **III** with acetic anhydride in pyridine at room temperature afforded diacetylpluramycin A (**IV**), mp 144~146°C (dec.), *m/e* 856 (M^+ for $C_{47}H_{56}N_2O_{13}$). In ^1H NMR spectra of **III** and **IV** (Table 1), the relation of protons in a series of CH_3-CH=CH-CH-[(C-19)-(C-18)-(C-17)-(C-16)-] was carefully analyzed. On NOE experiments of **III**, saturation of the $15CH_3$ singlet resulted in enhancements of 26% and 16% of the integrated areas of 3-H and 16-H, respectively, suggesting that the side chain at C-2 has an oxirane ring on C-14 and C-16[5]. Saturation of the $13CH_3$ singlet indicated a 26% NOE for 6-H, and an NOE on 6′-H or 6″-H upon irradiation of the 9-H singlet was also observed.

In ^{13}C NMR spectrum of **III**, all carbons except for N-methyl carbons were completely assigned by off-resonance decoupling, selective proton decoupling and gated decoupling techniques, as shown in Table 2. The identification of C-12a (δ 119.1) was made by a long-range coupling with 6-H, and then a signal at δ 116.0 was assigned to C-11a. Since the C-16 signal at δ 61.7 had a large ^{13}C-^1H coupling constant, J=174 Hz, the existence of the oxirane ring on C-14 and C-16 could be confirmed[6].

Therefore, the structure **III** can be assigned to pluramycin A. The stereochemistry of the olefin on the side chain is shown to be *trans* by the coupling constant of the olefinic protons and the long-range coupling between 17-H and $19CH_3$. The NOE experiment can suggest the *cis* configuration for the epoxide, but its absolute

Table 2. The ^{13}C chemical shifts of neopluramycin (**I**), pluramycin A (**III**) and their diacetates (**II** and **IV**).

Carbon	(ppm)			
	I	II	III	IV
2′	77.7 d	(73.0)	77.6 d	(73.0)d
3′	71.8 d	(75.8)	70.6 d	(75.8)d
4′	67.5 d	64.7	68.1 d	64.7 d
5′	41.0 t	42.0	38.8 t	42.0 t
6′	75.4 d	(75.4)	74.0 d	(75.4)d
2′-Me	18.9 q	18.5	18.5 q	18.4 q
3′-OCO-		(169.0)		(169.1)s
3′-OCOMe		(21.2)		(21.2)q
4′-NMe_2	(40.5)q	(40.7)	(40.4)q	(40.7)q
2″	69.8 d	70.2	69.8 d	70.2 d
3″	76.4 d	75.8	74.5 d	75.8 d
4″	57.6 s	57.8	59.1 s	57.9 s
5″	28.6 t	31.5	30.4 t	31.6 t
6″	64.9 d	64.7	65.7 d	64.7 d
2″-Me	15.0 q	14.8	15.1 q	14.8 q
4″-Me	13.7 q	13.8	13.9 q	13.9 q
3″-OCO-	170.6 s	170.3	171.0 s	170.3 s
3″-OCOMe	21.3 q	(21.3)	21.5 q	(21.3)q
4″-NMe_2	(39.3)q	(39.1)	(38.8)q	(39.1)q
2	159.3 s	155.7	159.6 s	155.1 s
3	108.8 d	108.7	109.9 d	109.5 d
4	179.5 s	179.8	178.8 s	179.0 s
4a	126.2 s	(127.0)	126.4 s	(126.1)s
5	149.6 s	148.2	150.0 s	148.3 s
6	125.4 d	124.4	125.9 d	124.9 d
6a	137.2 s	136.7	137.0 s	136.7 s
7	183.3 s	184.2	183.5 s	184.1 s
7a	127.3 s	(127.6)	126.5 s	(128.5)s
8	140.6 s	143.6	140.0 s	143.7 s
9	132.6 d	130.8	132.2 d	130.9 d
10	138.5 s	128.6	137.0 s	128.5 s
11	163.9 s	144.4	167.6 s	144.4 s
11a	115.8 s	(127.6)	116.0 s	(127.2)s
12	188.0 s	170.6	187.7 s	170.5 s
12a	118.9 s	121.0	119.1 s	121.3 s
12b	155.8 s	145.3	156.0 s	145.2 s
13	24.1 q	23.8	24.2 q	23.9 q
14	125.9 s	125.9	60.3 s	58.9 s
15	15.0 q	14.8	14.9 q	14.1 q
16	134.2 d	133.3	61.7 d	61.9 d
17	12.1 q	12.0	123.3 d	123.4 d
18			134.1 d	133.8 d
19			14.4 q	13.9 q
11-OCO-		(163.7)		(167.4)s
11-OCOMe		(21.2)		(21.2)q

The ^{13}C FT NMR spectra were taken with a Varian XL-100 spectrometer. Sample were dissolved in $CDCl_3$ containing TMS as the internal reference. Assignments, s, d, t and q, show multiplicity on off-resonance experiment. Similar values in parentheses within each column may be interchanged; their tentative assignments are given on the basis of the values of **III**.

structure is remained without determination.

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