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STEREOCHEMISTRY OF MACROLIDES—IV[1]

CONFORMATIONAL STUDIES ON 14-MEMBERED MACROLIDE—"DIAMOND LATTICE" CONFORMATION MODELS

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Abstract—Conformations of 14-membered macrolide—pikromycin, narbomycin, and their derivatives—in solution are studied based upon their NMR and CD spectra compared with the conformation of *p*-bromobenzoylpikromycin in solid state. The α,β-unsaturated CO group at the C-9 position in pikromycin, acetylpikromycin, *p*-bromobenzoylpikromycin, diacetylpikromycin, pikronolide, narbomycin and narbonolide has an *s-trans* conformation in solution of the protic solvent. While, in pikromycin, acetyl pikromycin, and *p*-bromobenzoylpikromycin, it has an *s-cis* conformation in solution of the aprotic solvent. This phenomenon has not been reported previously in macrolides, and is caused by an intramolecular H-bond between the OH group at the 12-position and the C-3 CO group in the aprotic solvent. This was confirmed from NMR, IR, and CD spectra.

The conformation of the 14-membered macrolactone is discussed with reference to "diamond lattice" conformation models A, B, C, D, and F. A new "diamond lattice" conformation model E for pikromycin in the aprotic solvents is proposed based on spectral data.

There are many reports on conformational studies on erythromycins from NMR[2] and CD[3] spectra. Celmer[4] has proposed a similar conformation for the macrolactone ring in oleandomycin. Recently, Egan *et al.*[5] reported that the conformation of the 14-membered macrolactone ring in erythronolide B, were relatively flexible. This conformational moving was confirmed by CMR spectra.[6] Previously,[1] we discussed similar conformational moving in oleandomycin and its derivatives based on the X-ray analysis of 11,4″-bis[*O*-(*p*-bromobenzoyl)]oleandomycin.

"Diamond lattice" conformation models

The application of Dale's "diamond lattice" conformation model[7] A (Diamond Model A) to 14-membered macrolide antibiotics was proposed earlier by Celmer.[8] Egan *et al.*[5,9] subsequently proposed an alternate "diamond lattice" conformation model B (Diamond Model B) to be applied to the 14-membered macrolactone of erythromycin[5,9] and lankamycin[10] antibiotics.

Recently, we proposed another "diamond lattice" conformation model F (Diamond Model F) instead of the Diamond Models A and B for 14-membered macrolactone of oleandomycin and erythromycin antibiotics based on the X-ray analysis of 11,4″-bis[*O*-(*p*-bromobenzoyl)]oleandomycin.[1]

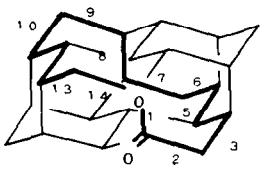
In this paper, we would like to report the conformational flipping of 14-membered macrolactone of pikromycin derivatives, comparing the conformational moving of oleandomycin antibiotics and using the "diamond lattice" conformation models (Diamond Models). The conformational relationship between the Diamond Models A, B, and F is clearly shown by the maps of dihedral angles in Fig. 1.

In an earlier paper, we proposed the application of a "diamond lattice" conformation model C[11] (Diamond Model C) to the 14-membered macrolactone of kromycin (**7**), 10,11-dihydrokromycin, deoxykromycin, and 10,11-dihydrodeoxykromycin on the basis of the X-ray analysis of kromycin (**7**).[12] It is clear that the Diamond Model C fits the conformation of **7**. **8** and this is proved by the maps of dihedral angles shown in Fig. 2. Evidently, the shape and each dihedral angle determined by X-ray analysis (dotted line) are in accord with those estimated from the Diamond Model C (solid line).

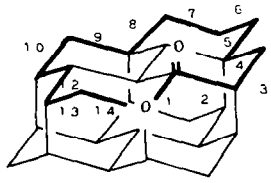
Recently, a new "diamond lattice" conformation model D (Diamond Model D) for the 14-membered macrolactone of *p*-bromobenzoylpikromycin (**5**) was proposed based on the X-ray analysis.[13] In Fig. 3 shows that the Diamond Model D applied to **5** based on the X-ray analysis. It is clear that the shape and each dihedral angle determined by X-ray analysis (dotted line) are in accord with those estimated from the Diamond Model D (solid line).

Chemistry

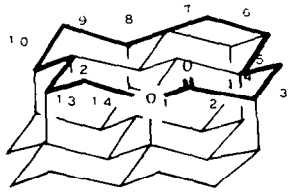
Pikromycin[14] (**1**) was obtained from the fermentation broth of *Streptomyces flavochromogenese*,[15] and narbomycin (**2**), pikronolide (**9**)[16] and narbonolide



Diamond Model A



Diamond Model B



Diamond Model F

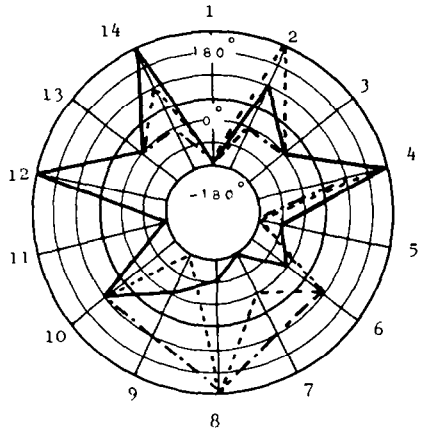
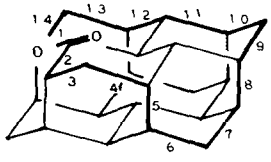


Fig. 1. Diamond model A, B, F and maps of dihedral angles (A, B, F).



Diamond Model C

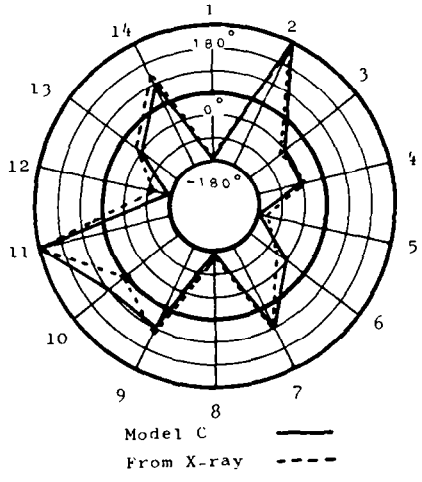
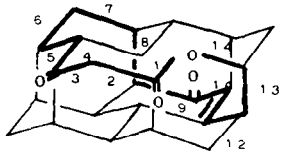


Fig. 2. Diamond Model C and maps of dihedral angles.



Diamond Model D

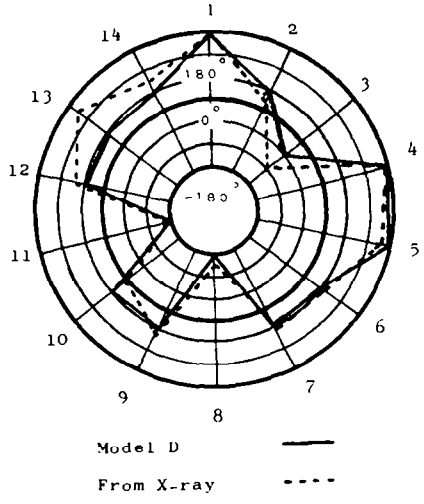
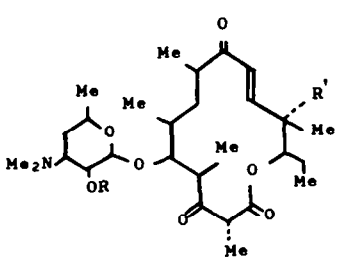
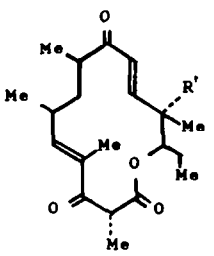
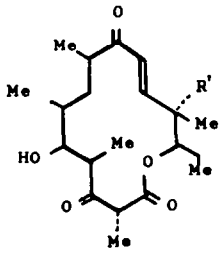


Fig 3. Diamond Model D and maps of dihedral angles







1	R=H	R'=OH	7	R'=OH	9	R'=OH
2	R=H	R'=H	8	R'=H	10	R'=H
3	R=$COCH_3$	R'=OH				
4	R=$COCH_3$	R'=$OCOCH_3$				
5	R=p-bromobenzoyl	R'=OH				
6	R=$COCH_3$	R'=H				

Chart 1.

(**10**)[17] were obtained from the fermentation broth of *Streptomyces venezuelae* MCRL-0376.

Acetylpikromycin (**3**) was prepared from **1** with acetic anhydride in dry benzene solution, and diacetylpikromycin (**4**) was obtained from **1** with acetic anhydride in pyridine at room temperature. Easy acetylation of the tertiary hydroxyl group at 12-position of **1** may be explained by the small steric hindrance because of the bridge-head position. For a similar reason, acetylation of a tertiary hydroxyl group was reported in steroids[18] and sugar derivatives.[19] Acetylnarbomycin (**6**) was prepared by a similar procedure to that for **4**.

Stereochemistry in solution

Fig. 4 shows the CD curves of pikromycin (**1**), acetylpikromycin (**3**), diacetylpikromycin (**4**), pikronolide (**9**), narbomycin (**2**), acetylnarbomycin (**6**), and narbonolide (**10**). The n-π^* Cotton effect owing to a carbonyl group at 3-position appeared around

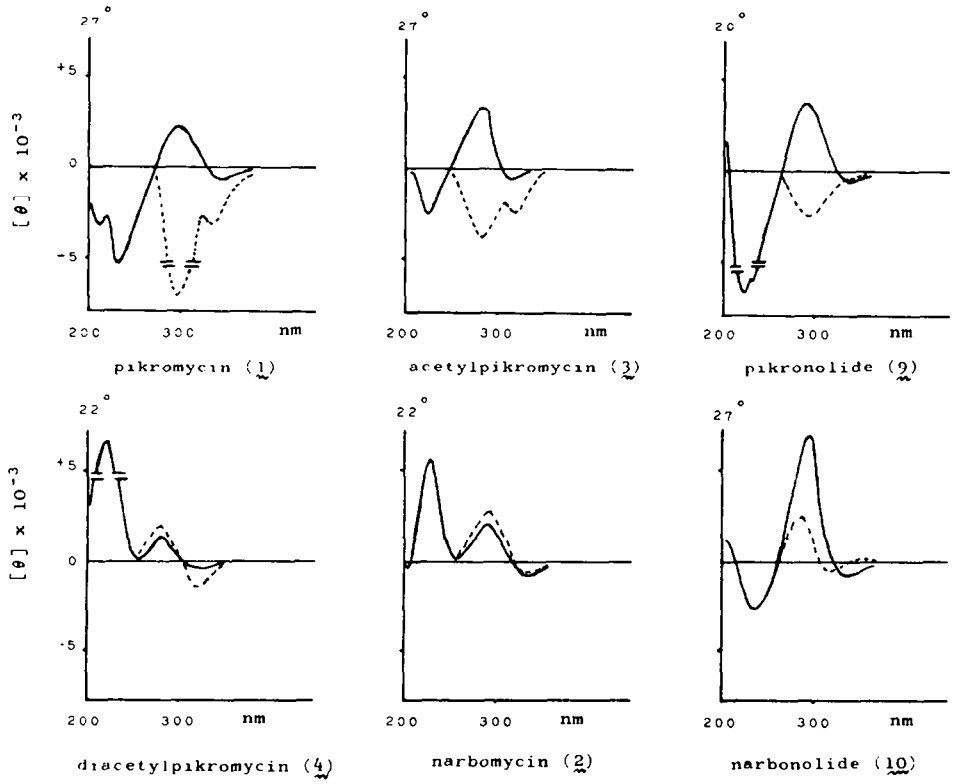


Fig. 4. CD curves in MeOH (·——) and $CHCl_3$ (· - -).

280–290 nm and it should be noted that the sign of the effect changes according to different solvents in some cases.

The reversal of the sign of the n-π^* Cotton effect at about 290 nm was observed in pikromycin (**1**), acetylpikromycin (**3**), and pikronolide (**9**) by changing solvents. In methanol, the positive Cotton effect was observed with pikromycin, narbomycin and their derivatives as shown in Fig. 4. While, in chloroform or ether, the negative Cotton effect was observed with pikromycin (**1**), monoacetylpikromycin (**3**), and pikronolide (**9**). This phenomenon is clearly detected by adding methanol in ether solution as shown in Fig. 5. Low temperature CD curves of pikromycin (**1**) and narbomycin (**2**) are shown in Fig. 6. The conformation of their 14-membered macrolactone is more rigid under low temperature.

This can be explained by the intramolecular H-bonding between the CO group at 3-position and the OH group at 12-position. When the OH group is acetylated or replaced by H—namely, narbomycin and its derivatives—the same positive Cotton effects were observed at around 280–290 nm both in methanol and in chloroform. The above discussion can probably be explained by octant projection A (positive Cotton effect) and B (negative Cotton effect).

IR data of the CO group in carbon tetrachloride can be used for detecting the intramolecular H-bonding. In pikromycin (**1**), a strong absorption at 1750 cm^{-1} is assigned to a lactone CO and a strong absorption at

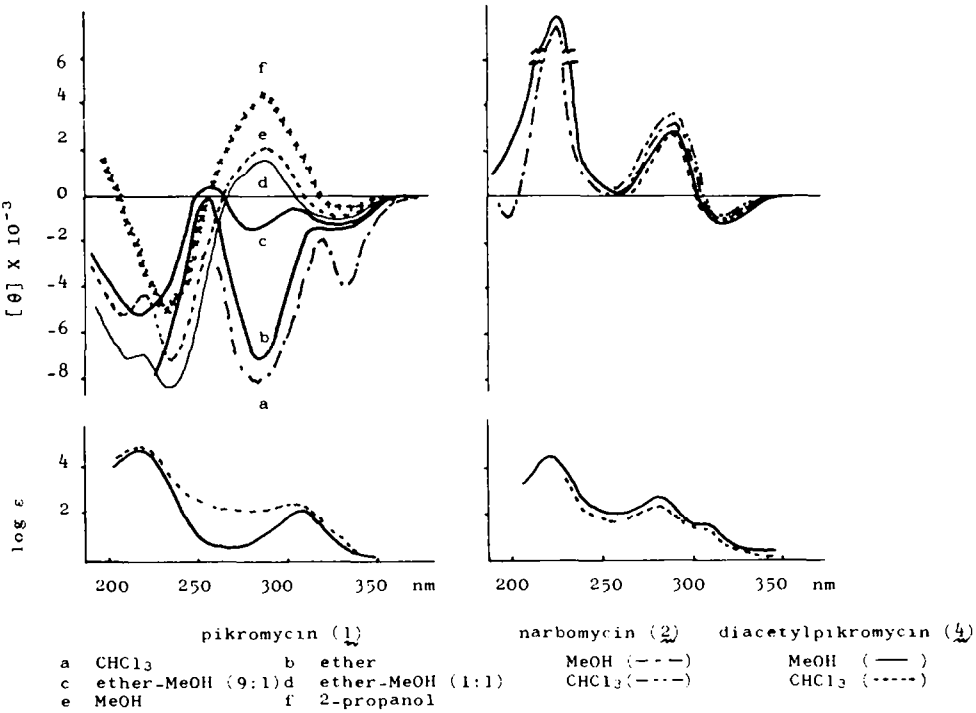


Fig. 5. CD curves of **1**, **2**, and **4** in various solvents.

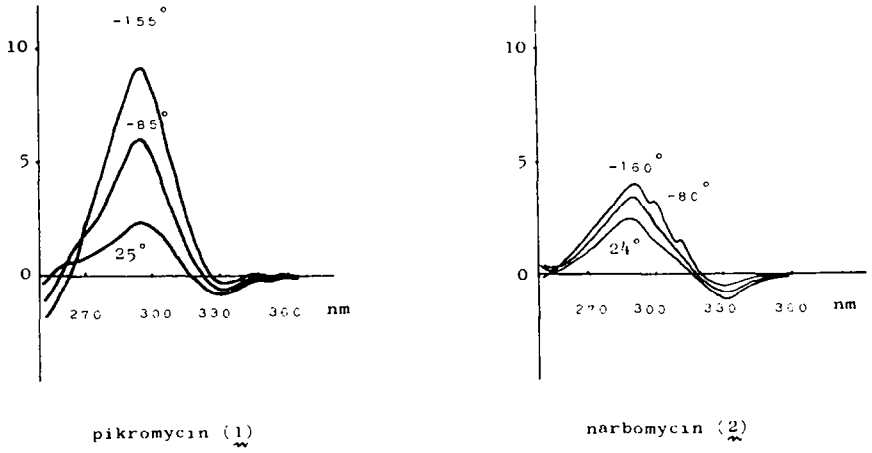


Fig. 6. CD curves of **1** and **2** at low temperatures (EtOH:MeOH = 1:1).

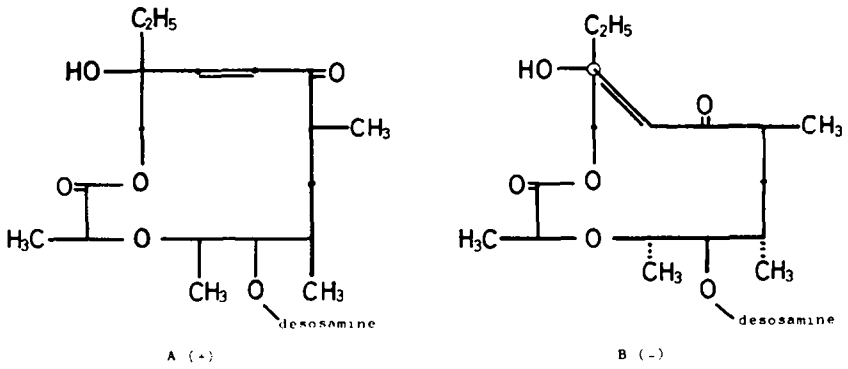


Fig. 7. Octant projections at C-3 position.

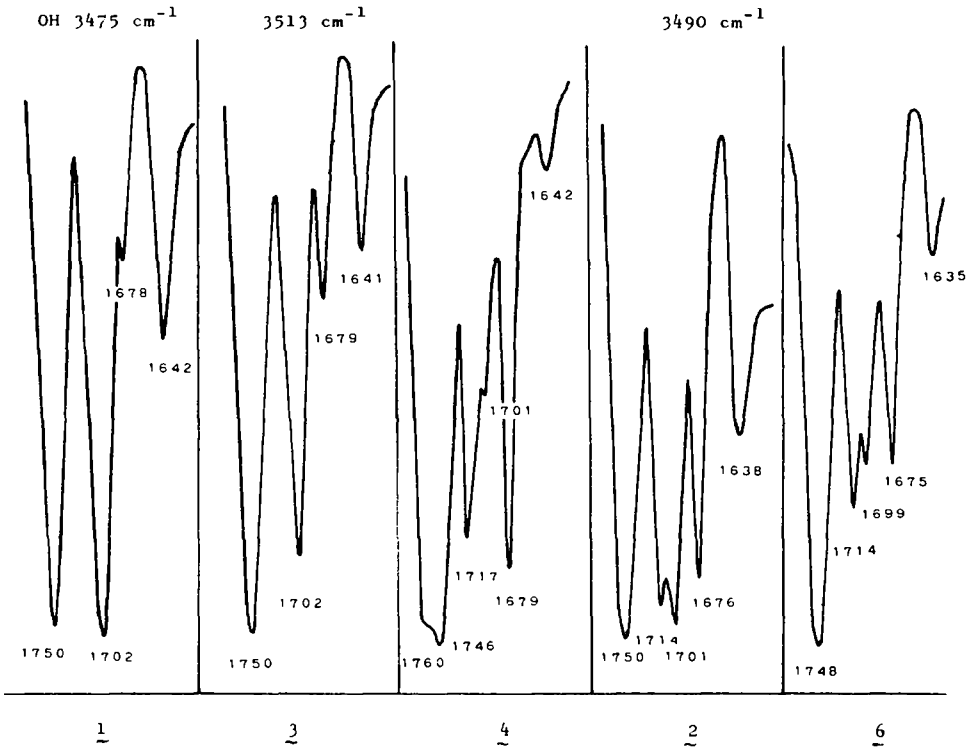


Fig. 8. IR spectra in CCl_4 solution (0.002 M) by 1 cm cell.

1702 cm^{-1} to a chelate CO at 3-position, respectively. Two bands at 1678 and 1642 cm^{-1} are assigned to an unsaturated CO group at 9-position.

A similar IR absorption band in carbon tetrachloride for the chelate carbonyl at 3-position of monoacetylpikromycin (**3**) appeared at 1702 cm^{-1}. But in diacetylpikromycin (**4**), the chelate CO band shifted about 15 cm^{-1} to a shorter wavelength and appeared at 1717 cm^{-1}. This band appeared in narbomycin and acetylnarbomycin (**6**) at 1714 cm^{-1}.

From these observations, it is concluded that an intramolecular H-bonding is formed between the CO group at 3-position and the OH group at 12-position. Medium strong bands appeared at 1678 and 1642 cm^{-1} in pikromycin (**1**), and at 1679 and 1641 cm^{-1} in acetylpikromycin (**3**), respectively, from which the conformation of the unsaturated CO group at 9-position is suggested to be the *s-cis* conformation. This hypothesis of *s-cis* conformation explains the reversal of the sign of the Cotton effect in protic solvent and aprotic solvent. In aprotic solvent, the intramolecular H-bond formation causes a part of ring flip at position 10–11 and the conformation changes from *s-trans* to *s-cis*.

This is further supported by the NMR spectra. From CMR, the Me group shows much shift by acetylation. This was also reported in erythromycin and oleandomycin derivatives.[1] The proton coupling constants of pikromycin (**1**) in aprotic solvent are $J_{4,5} = 7.0$ Hz and $J_{5,6} = 2.5$ Hz ($CDCl_3$ and C_6D_6). On the other hand, in protic solvent the values change

Table 1. Chemical schifts (δ:ppm) and coupling constants (Hz) of pikromycin (**1**) in various solvents

Solvent	$CDCl_3$	C_6D_6	CD_3OD	C_5D_5N		
				-20°	32°	100°
4-H ($J_{4,5}$)	3.20 (7.0)	3.13 (7.0)	3.04 (5.5)	3.15 (5.6)	3.12 (6.5)	3.02 (6.5)
5-H ($J_{5,6}$)	3.95 (2.5)	3.71 (2.5)	4.01 (2.0)	4.02 (2.0)	4.34 (2.2)	4.18 (2.2)
10-H ($J_{10,11}$)	6.28 (16.0)	6.49 (16.0)	6.22 (16.0)	6.32 (16.0)	6.63 (16.0)	6.93 (16.0)
11-H ($J_{11,10}$)	6.63 (16.0)	6.84 (16.0)	6.69 (16.0)	6.71 (16.0)	7.22 (16.0)	7.02 (16.0)

to $J_{4,5} = 5.5$ Hz and $J_{5,6} = 2.0$ Hz (CD_3OD). In narbomycin (**2**) and diacetylpikromycin (**4**), the values were the same in $CDCl_3$ and CD_3OD, that is, $J_{4,5} = 6.0$ and 5.0, $J_{5,6} = 2.0$ Hz, respectively, and these values are similar to those of pikromycin (**1**) in methanol.

Observed NOE's in benzene also support the *s-cis* conformation of pikromycin (**1**) in aprotic solvent. The NOE's (Fig. 9) were observed between 4-CH_3 and 10-H ($6 \pm 2\%$), between 8-H and 10-H ($15 \pm 4\%$), and between 11-H and 12-CH_3 ($16 \pm 3\%$) in C_6D_6. Similar conclusion was obtained in $CDCl_3$ and C_5D_5N summarized in Table 2. The NOE's between 4-Me and 10-H, and between 11-H and 12-Me were confirmed by the application of the homonuclear INDOR technique. The chemical shift of 10-H (6.28 ppm) to a higher field was more than that of 11-H (6.63 ppm). These data suggested the *s-cis* conformation for the α,β-unsaturated CO group at C-9 position.

On the other hand, observed NOE between 8-H and 11-H in CD_3OD supports the *s-trans* conformation of

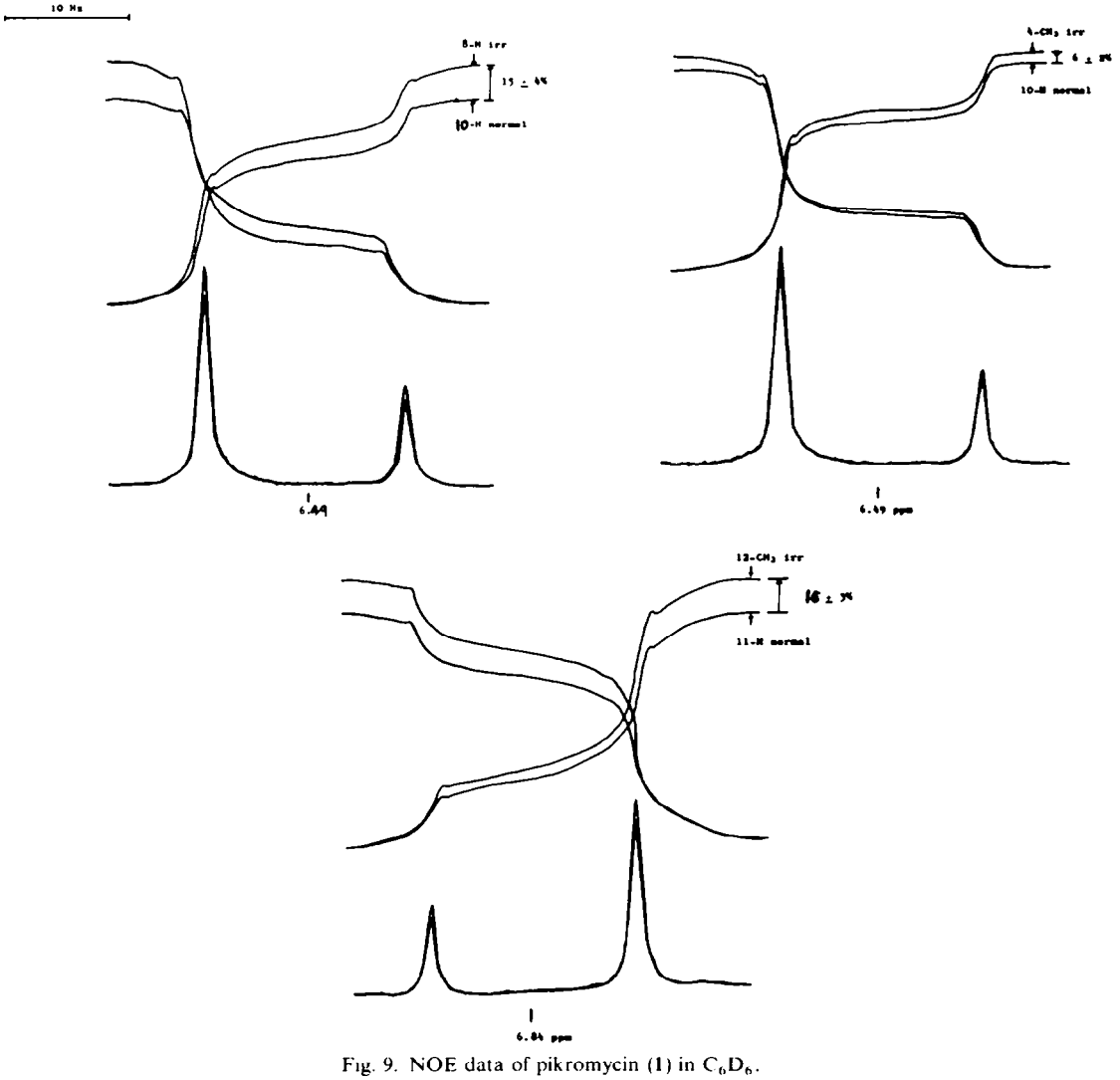
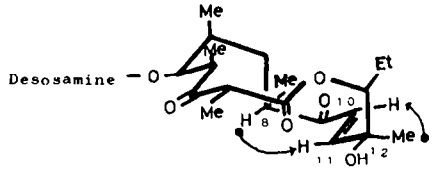
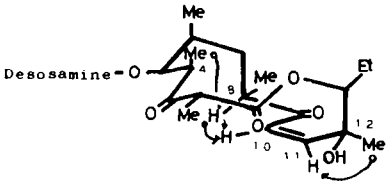


Fig. 9. NOE data of pikromycin (**1**) in C_6D_6.

Table 2. Data of NOEs in various conditions



Diamond Model D



Diamond Model E

	solvent	[8-H]→11-H	[12-Me]→10-H	pikromycin solvent	[8-H]→10-H	[12-Me]→11-H	[4-Me]→10-H
pikromycin	CD_3OD	15%	12%	C_6D_6	15%	16%	6%
diacetylpikromycin	$CDCl_3$	17	20	$CDCl_3$	18	12	6
narbomycin	$CDCl_3$	-	11	C_5D_5N (-20°)	18	14	6
narbonolide	$CDCl_3$	10	15	" (32°)	15	13	6
				" (100°)	12	11	6

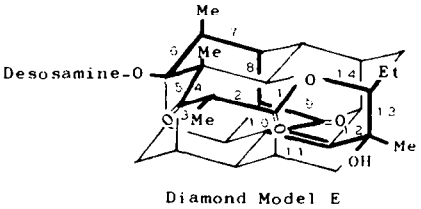
1 in protic solvent. A similar result was obtained in diacetylpikromycin (**4**; 17% between 8-H and 11-H, 20% between 12-Me and 10-H), narbomycin (**2**; 11% between 12-Me and 10-H), and narbonolide (**10**; 10% between 8-H and 11-H, 15% between 12-Me and 10-H).

The J values of **1** in C_6D_6, $J_{13,14}$ = 2 and 11 Hz at 5.12 ppm revealed that the ethyl group at C-13 position was hindered from free-rotation by the steric hindrance of the 12-OH group. This tendency was also observed in acetylpikromycin (**3**) ($J_{13,14}$ = 2.5 and 11 Hz) and pikronolide (**9**) ($J_{13,14}$ = 3 and 10 Hz). This result was confirmed from the comparison of the J values of **1**, **3**, and **9** with those of narbomycin (**2**) ($J_{13,14}$ = 6 and 8 Hz), which showed a poorly split d-doublet when irradiated at 14-CH_2 protons, and from the high-temperature NMR studies on **1** (Table 3). These data show that the steric hindance of 12-OH group affected the free rotation of the 13-Et group, but did not hinder it completely.

In conclusion, the most favorable new "diamond lattice" conformation model E (Diamond Model E) is proposed for pikromycin (**1**), acetylpikromycin (**3**), *p*-bromobenzoylpikromycin (**5**), and pikronolide (**9**) in

Table 3. NMR data of pikromycin (**1**) at 13-H in various conditions (δ:ppm: Hz)

Temp. / Solv.	25°	50°	80°	100°	120°	149°
$CDCl_3$	5.00(11.1/2.8)	4.98(11.5/3.0)	4.98(11.2/3.0)	4.97(10.5/3.2)	-	-
C_6F_6	4.93(11.0/3.2)	4.93(11.0/3.2)	4.93(11.5/3.5)	4.93(11.5/3.5)	-	-
$CHBr_3$	-	-	-	-	- (10.0/3.0)	- (9.9/3.2)



Diamond Model E

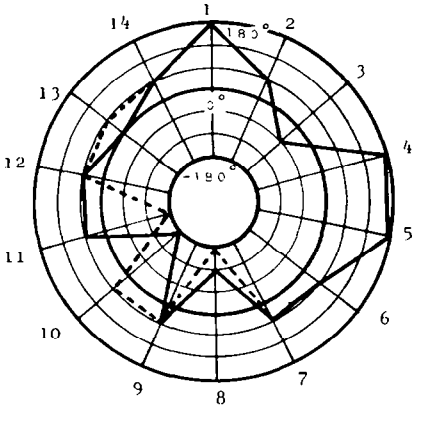


Fig. 10. Diamond Model E and maps of dihedral angles (D, E).

aprotic solvent such as chloroform, ether and pyridine. The Diamond Model E can explain NMR and CD data, and *s-cis* conformation of the α,β-unsaturated CO group at C-9 position.

EXPERIMENTAL

Temps are uncorrected. NMR spectra were measured with a Varian HA-100 and JEOL PS-100 spectrometers operating in frequency sweeps at 32 and 25°, respectively, with internal TMS- or benzene-locked mode. Chemical shifts are recorded in ppm (δ) and coupling constants are recorded in Hz. Mass spectra were determined with a JEOL 01S spectrometer by a direct inlet system at 75 eV. IR spectra were recorded with a Shimadzu IRG-1 (KBr) and with a Japan Spectroscopic Model DS-701G in CCl_4 and 1 cm cell was used for the intramolecular H- bond measurements. CD data were obtained on a Japan Spectroscopic Model J-20 recording polarimeter.

Acetylpikromycin (**3**). Soln of **1** (100 mg) in dry benzene (10 ml) and Ac_2O (1 ml) was left at room temp for 10 min. After decomposition of excess reagent, the solvent was evaporated under a reduced pressure. The residue was dissolved in ether, and washed with $NaHCO_3$aq and water. Evaporation of dried ethereal soln left **3** (92 mg) as a white powder: IR (KBr) 1750, 1702, 1679, 1641 cm^{-1} (CO); UV λ_{max}^{EtOH} 225 nm (log ε 4.02). (Found: C, 63.42; H, 8.74; N, 2.45. Calc. for $C_{30}H_{49}NO_9$: C, 63.47; H, 8.70; N, 2.47%).

Diacetylpikromycin (**4**). Soln of **1** (100 mg) in pyradine and Ac_2O (1 ml) was left at room temp for 2 hr. After decomposition of excess reagent, the mixture was extracted with $CHCl_3$. Evaporation of the dried $CHCl_3$ soln left **4** (80 mg) as a white powder: IR (KBr) 1750, 1745, 1717, 1710, 1679, 1642 cm^{-1} (CO); UV λ_{max}^{EtOH} 225 nm (log ε 4.10). (Found:

Table 4. NMR data of pikromycin (**1**)

	Chemical shifts (δ ppm; J value, Hz)			
	C_6D_6	$CDCl_3$	$\Delta^{CDCl_3}_{C_6D_6}$	CD_3OD
2-H	4.01, q, $J_{2,2Me}$=7.2	3.89	-0.12	(4.07)
2-Me	1.38, d, J=7.2	1.47	0.09	1.33
4-H	3.13, dq, $J_{4,5}$=7.0; $J_{4,4Me}$=6.8	3.20	0.07	3.04
4-Me	1.20, d, J=6.8	1.31	0.11	1.30
5-H	3.71, dd, $J_{5,4}$=7.0; $J_{5,6}$=2.5	3.95	0.24	4.01
6-H	2.2, m, $J_{6,5}$=2.5; $J_{6,6Me}$=7.0	2.1		
6-Me	1.05, d, $J_{6Me,6}$=7.0	1.05	0	1.01
8-H	2.61, m, $J_{8,8Me}$=6.5	2.70	0.09	2.76
8-Me	1.24, d, J=6.5	1.10	-0.14	1.09
10-H	6.49, d, $J_{10,11}$=16.0	6.28	-0.21	6.22
11-H	6.84, d, $J_{11,10}$=16.0	6.63	-0.21	6.69
12-OH				
12-Me	1.13, s	1.33	0.20	1.33
13-H	5.12, dd, $J_{13,14}$=11 and 2	5.01	-0.11	4.87
14-H	(1.3), t, $J_{14Me,14}$=7.0	1-1.8		
14-Me	0.73, t, $J_{14Me,14}$=7.0	0.88	0.15	0.90
1'-H	4.25, d, $J_{1',2'}$=7.5	4.36	0.11	4.30
2'-H	3.17, dd, $J_{2',1'}$=7.5; $J_{2',3'}$=10.3	3.24	0.07	3.27
3'-H	2.16, m, $J_{3',2'}$=10.3; $J_{3',4'}$=4 and 12	2.48	0.32	2.61
NMe_2	1.88, s	2.28	0.40	2.33
4'-H	1.5, m			
5'-H	3.20, m, $J_{5',4'}$=2 and 10.5; $J_{5',5'Me}$=6.0	3.56	0.36	3.57
5'-Me	1.05, d, $J_{5'Me,5'}$=6.0	1.24	0.19	1.22

Table 5. NMR data of acetylpikromycin (**2a**) and diacetylpikromycin (**3**)

	Chemical shifts ($CDCl_3$, δ ppm; J value, Hz)	
	2a	**3**
2-H	3.75, q, $J_{2,2Me}$=7.2	3.81, q, $J_{2,2Me}$=7.0
2-Me	1.43, d, J=7.2	1.39, d, J=7.0
4-H	2.96, dq, $J_{4,5}$=5.5; $J_{4,4Me}$=7.0	2.80, dq, $J_{4,4Me}$=7.3; $J_{4,5}$=4.5
4-Me	1.23, d, J=7.0	1.24, d, $J_{4Me,4}$=7.3
5-H	4.18, dd, $J_{5,4}$=5.5; $J_{5,6}$=2.5	4.40 dd, $J_{5,4}$=4.5; $J_{5,6}$=2.0
6-H		2.30
6-Me	0.98, d, $J_{6Me,6}$=7.2	0.95, d, J=6.7
7-H_2		6.42
8-H	2.85	3.07
8-Me	1.11, d, $J_{8Me,8}$=6.5	1.12, d, J=6.5
10-H	6.17, d, $J_{10,11}$=17	5.86, d, $J_{10,11}$=17.0
11-H	6.56, d, $J_{11,10}$=17	6.42, d, $J_{11,10}$=17.0
12-H		
12-OH		
(OAc)		(2.10, s)
12-Me	1.34, s	1.59, s
13-H	4.99, dd, $J_{13,14}$=11 and 2	5.29, dd, $J_{13,14}$=10.5 and 3
14-H_2	1.8 2	
14-Me	0.88, t, $J_{14Me,14}$=7.0	0.88, t, $J_{14Me,14}$=7.0
1'-H	4.52, d, $J_{1',2'}$=7.5	4.52, d, $J_{1',2'}$=7.5
2'-H	4.82, dd, $J_{2',1'}$=7.5; $J_{2',3'}$=10.5	4.81, dd, $J_{2',1'}$=7.5; $J_{2',3'}$=10.3
2'-OH		
(OAc)		(1.98, s)
3'-H	2.85	2.75, m, $J_{3',2'}$=10.3; $J_{3',4'}$=12.3 and 4.5
NMe_2	2.34, s	2.26, s
5'-H	3.59, m, $J_{5',4'}$=1.2 and 10	3.61, m, $J_{5',4'}$=10.5 and 2.0
5'-Me	1.27, d, $J_{5'Me,5'}$=6	1.27, d, $J_{5'Me,5'}$=6.0

Table 6. NMR data of narbomycin (**5**) and narbonolide (**7a**)

	Chemical shifts (δ ppm; J value, Hz)				
	5			**7a**	
Solvent	$CDCl_3$	C_6D_6	$\Delta^{CDCl_3}_{C_6D_6}$	$CDCl_3$	$\Delta^{CDCl_3}_{C_6D_6}$
2-H	3.85, q, $J_{2,2Me}$=7.0	3.69	0.16	3.71	0.25
2-Me	1.37, d, J=7.0	1.33	0.04	1.35	0.10
4-H	2.94, dq, $J_{4,5}$=6; $J_{4,4Me}$=7.4	2.94	0	2.69	0.21
4-Me	1.37, d, J=7.4	1.24	0.13	1.13	0.09
5-H	4.16, dd, $J_{5,4}$=6; $J_{5,6}$=2	4.44	-0.28	3.87	-0.02
5-OH				2.28	0.13
6-H	1.72, dd, $J_{6,5}$=2; $J_{6,6Me}$=7	ca2.1	ca-0.4		
6-Me	1.03, d, J=7	1.12	-0.09	0.94	0.03
8-H	2.7	2.94	ca-0.2	2.99	0
8-Me	1.12, d, $J_{8Me,8}$=6.5	1.44	-0.22	1.10	0.02
10-H	6.12, dd, $J_{10,11}$=16; $J_{10,12}$=1.5	6.16	-0.04	6.10	0.07
11-H	6.66, dd, $J_{11,10}$=16; $J_{11,12}$=6.3	6.72	-0.06	6.88	0.15
12-H	2.74, m, $J_{12,10}$=1.5; $J_{12,11}$=6.3; $J_{12,12Me}$=7.0	2.47	0.27	2.69	0.53
12-Me	1.10, d, $J_{12Me,12}$=7.0	0.72	0.38	1.13	0.38
13-H	4.91, m, $J_{13,12}$=3.5; $J_{13,14}$=6 and 8	4.82	0.09	5.13	0.27
$14-H_2$	1.5±0.2				
14-Me	0.91, t, $J_{14Me,14}$=7	0.69	0.22	0.92	0.27
1'-H	4.30, d, $J_{1',2'}$=6.2	4.45	-0.15		
2'-H	3.24, dd, $J_{2',1'}$=6.2; $J_{2',3'}$=10.1	3.34	-0.10		
3'-H	2.49, m, $J_{3',2'}$=10.1; $J_{3',4'}$=4 and 12	2.21	0.28		
5'-H	3.55, m, $J_{5',4'}$=2.5 and 11	3.18	ca0.4		
5'-Me	1.25, d, $J_{5Me,5'}$=6.3	1.07	0.18		
2'-OH	3.13, s	3.34	ca-0.2		
NMe_2	2.28, s	1.88	0.40		

C, 62.80; H, 8.65; N, 2.30. Calc. for $C_{32}H_{51}NO_{10}$: C, 63.03; H, 8.43; N, 2.30%).

Acetylnarbomycin (**6**). Soln of **2** (30 mg) in pyridine (0.5 ml) and Ac_2O (0.5 ml) was left at room temp for 4 hr. After decomposition of excess reagent, the mixture was extracted with $CHCl_3$. Evaporation of the dried $CHCl_3$ soln left **6** (25 mg) as a white powder; IR (KBr) 1645 cm^{-1} (CO); UV λ_{max}^{EtOH} 225 nm (log ε 3.82); NMR ($CDCl_3$) δ 2.03 (3 H, s, OAc), 2.32 (6H, s, NMe_2), 3.82 (1 H, q, J = 7.8 Hz, 2-H), 6.01 (1 H, d, J = 16.5 Hz, 10-H), 6.62 (1 H, d-d, J = 16.5 and 6 Hz, 11-H). (Found: C, 64.99; H, 8.75; N, 2.32. Calc. for $C_{30}H_{49}NO_8$: C, 65.31; H, 8.95; N, 2.54%).

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