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(29) Compounds **6A, B, 16A, B, 7, 17, 8, 9,** and **13** are named as hydroazulene derivatives in the Experimental Section. This differs from the numbering used in the text and in the schemes where the compounds are treated as vellerane derivatives following the suggestion of Professor Sukh Dev.

Stereochemistry of Macrolides. 3. X-ray Crystal Structure Analysis of 11,4″-Bis[*O*-(*p*-bromobenzoyl)]oleandomycin

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Abstract: Molecular structures of oleandomycin and its derivatives both in solid and solution have been determined by means of X-ray analysis of 11,4″-bis[*O*-(*p*-bromobenzoyl)]oleandomycin and its CD and NMR spectra. It was shown that the compound, $C_{49}H_{67}O_{14}NBr_2 \cdot H_2O \cdot CH_3OH \cdot C_2H_5OH$, is orthorhombic with space group $P2_12_12_1$ and unit cell dimensions of a = 14.283 (8), b = 32.057 (12), and c = 12.767 (7) Å, V = 5843 Å^3, and Z = 4. The crystal structure was solved by the heavy-atom method and refined by the block-diagonal least-squares method including anisotropic thermal parameters to a final R value of 0.112. The absolute configuration of the macrolactone moiety of oleandomycin was determined to be 2*R*,3*S*,4*R*,5*S*,6*S*,10*R*,11*S*,12*R*,13*R*, based on the already determined configuration of the D-desosamine moiety. A new "diamond lattice" conformation model F for 11,4″-bis[*O*-(*p*-bromobenzoyl)]oleandomycin was proposed based on the results of X-ray analysis. Conformations of oleandomycin and its derivatives in solution were discussed on the basis of CD and NMR spectra.

Oleandomycin is a 14-membered macrolide antibiotic isolated by Celmer et al.[2] and its structure and configuration were reported by the same author.[3] In this paper, we wish to report the conformation of oleandomycin by means of an X-ray analysis of 11,4″-bis[*O*-(*p*-bromobenzoyl)]oleandomycin and propose a new "diamond lattice" conformation model F (diamond model F). In relation to the conformation in solid state, CD curves and NMR spectra of oleandomycin (**1**), 11,4″-bis[*O*-(*p*-bromobenzoyl)]oleandomycin (**2**), triacetyloleandomycin (**3**), and the diacetylanhydroaglycon (**4**) of oleandomycin elucidated the stereochemistry of the 14-membered macrolactone of oleandomycin derivatives in solution (see Figure 1).

Bis[*O*-(*p*-bromobenzoyl)]oleandomycins were obtained by treating a benzene solution of oleandomycin (**1**) with *p*-bromobenzoyl chloride and pyridine, and bis-benzoate **2** was isolated from the above reaction mixture by silica-gel column chromatography.

Crystals of the compound suitable to X-ray work were obtained from an ethanol–methanol (1:1) solution in the form of colorless prisms elongated along the *c* axis. The density was measured by the floatation method in an aqueous solution of potassium iodide. Preliminary cell dimensions were obtained from Weissenberg photographs.

Experimental Section

11,4″-Bis[*O*-(*p*-bromobenzoyl)]oleandomycin[4] (2). To a solution of oleandomycin (1 g) in benzene (100 mL), a mixture of *p*-bromobenzoyl chloride (0.5 g) in benzene (20 mL) and pyridine (0.5 mL) was added dropwise under cooling. The reaction mixture was kept at room temperature for 20 h and treated with methanol to decompose the excess reagent. After removal of the solvent, the residue was dissolved in minimum amount of water, neutralized with 2% $NaHCO_3$, and then extracted with chloroform. The chloroform extract was washed, dried, and evaporated to leave a white powder. The bis-benzoate mixture thus obtained was purified by silica-gel chromatography. Elution with benzene–acetone (9:1) and evaporation of the eluate left white powder, and a second recrystallization from ethanol–methanol gave 150 mg of **2** as colorless prisms: mp 109–110 °C; IR ν_{max}^{KBr} 3420 (OH), 1745 (ester), 1720 (ketone), 1610 and 1590 cm^{-1} (phenyl); UV λ_{max}^{MeOH} 243.0 nm (log ϵ 4.27). Anal. Calcd for $C_{49}H_{67}O_{14}NBr_2 \cdot H_2O \cdot CH_3OH \cdot C_2H_5OH$: C, 54.22; H, 7.09; N, 1.22. Found: C, 54.15; H, 7.11; N, 1.23.

Diacetylanhydroaglycon (4) of Oleandomycin. The anhydroaglycon of **1** was prepared from **1** (0.85 g) according to modified procedures of Hochstein et al.[5] The yield was 0.072 g, mp 219–220 °C (lit.[5] mp 228–230 ° C). The diacetate **4** was prepared from the anhydroaglycon (0.05 g) by treating with acetic anhydride (1 mL) and pyridine (1 mL) at 60 °C. Recrystallization of the product from ether yielded 0.02 g (32%) of **4** as colorless needles: mp 196–197 °C; IR ν_{max}^{KBr} 1725 (ester), 1692 and 1640 cm^{-1} (α,β-unsaturated ketone); UV λ_{max}^{MeOH} 234.0 nm (log ϵ 4.12); CD (MeOH) $[\theta]^{20}_{333}$ −1194, $[\theta]_{294}$ 1683, $[\theta]_{233}$ 27 151; NMR[6] ($CDCl_3$, 100 MHz) δ 0.88 (3 H, d, $J_{4\text{-Me},4}$ = 7.0 Hz, 4-Me), 0.93 (3 H, d, $J_{6\text{-Me},6}$ = 7.0 Hz, 6-Me), 1.05 (3 H, d, $J_{12\text{-Me},12}$ = 7.0 Hz, 12-Me), 1.13 (3 H, d, $J_{2\text{-Me},2}$ = 7.0 Hz, 2-Me), 1.37 (3 H, d, $J_{13\text{-Me},13}$ = 6.5 Hz, 13-Me), 1.90 (1 H, m, 6-H), 1.92 (1 H, ddq, $J_{4,3}$ = 2.0 Hz, $J_{4,5}$ = 10.5 Hz, $J_{4,4\text{-Me}}$ = 7.0 Hz, 4-H), 1.98 (3 H, d, $J_{10\text{-Me},11}$ = 1.5 Hz, 10-Me), 2.69 (1 H, dd, $J_{2,3}$ = 8.5 Hz, $J_{2,2\text{-Me}}$ = 7.0 Hz, 2-H), 2.84 (1 H, d, $J_{14ax,14eq}$ = 5.5 Hz, 14-H_{ax}), 2.90 (1 H, d, $J_{14eq,14ax}$ = 5.5 Hz, 14-H_{eq}), 3.18 (1 H, ddq, $J_{12,11}$ = 10.7 Hz, $J_{12,13}$ = 4.5 Hz, $J_{12,12\text{-Me}}$ = 7.0 Hz, 12-H), 4.65 (1 H, dd, $J_{5,4}$ = 10.5 Hz, $J_{5,6}$ = 1.5 Hz, 5-H), 4.96 (1 H, dd, $J_{13,12}$ = 4.5 Hz, $J_{13,13\text{-Me}}$ = 6.5 Hz, 13-H), 5.09 (1 H, dd, $J_{3,2}$ = 8.5 Hz, $J_{3,4}$ = 2.0 Hz, 3-H), 6.54 (1 H, dq, $J_{11,12}$ = 10.7 Hz, $J_{11,10\text{-Me}}$ = 1.5 Hz, 11-H). Anal. Calcd for $C_{24}H_{36}O_8$: C, 63.56; H, 8.18. Found: C, 63.70; H, 8.02.

Crystal data for 11,4″-bis[*O*-(*p*-bromobenzoyl)]oleandomycin: mp 109–111 °C; $C_{49}H_{67}O_{14}NBr_2 \cdot H_2O \cdot CH_3OH \cdot C_2H_5OH$, MW 1150.1; orthorhombic; a = 14.283 (8), b = 32.057 (12), c = 12.767 (7) Å; V = 5843 Å^3; d_{obsd} = 1.295 g/cm^3, d_{calcd} = 1.310 g/cm^3; Z = 4; $F(000)$ = 2416; space group $P2_12_12_1$ (absent reflections; $h00$ when h is odd, $0k0$ when k is odd, and $00l$ when l is odd).

The diffraction intensities of a 0.2 × 0.3 × 0.4 mm^3 parallelpiped crystal were measured with a Rigaku four-circle diffractometer using graphite monochromated Cu Kα radiation. The accurate cell dimensions were determined by the least-squares method using the

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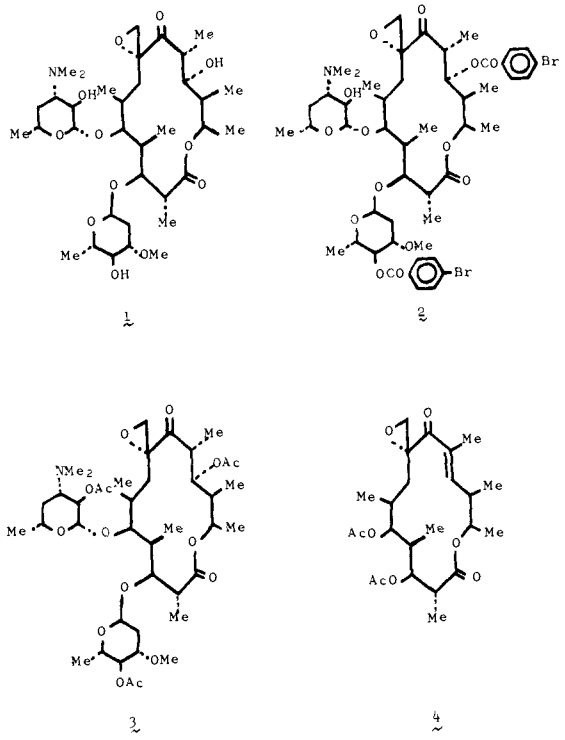


Figure 1.

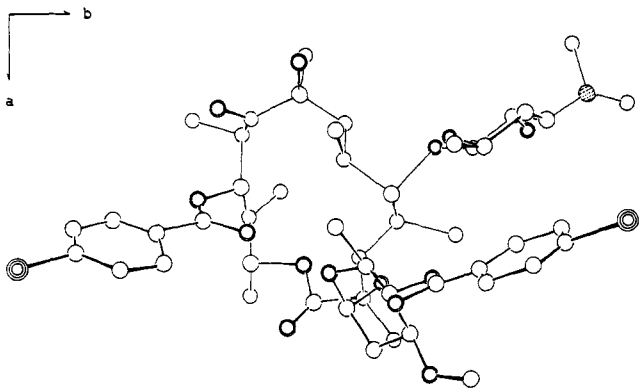


Figure 2. c-Axis projection of 11,4″-bis[O-(p-bromobenzoyl)]oleandomycin (**2**).

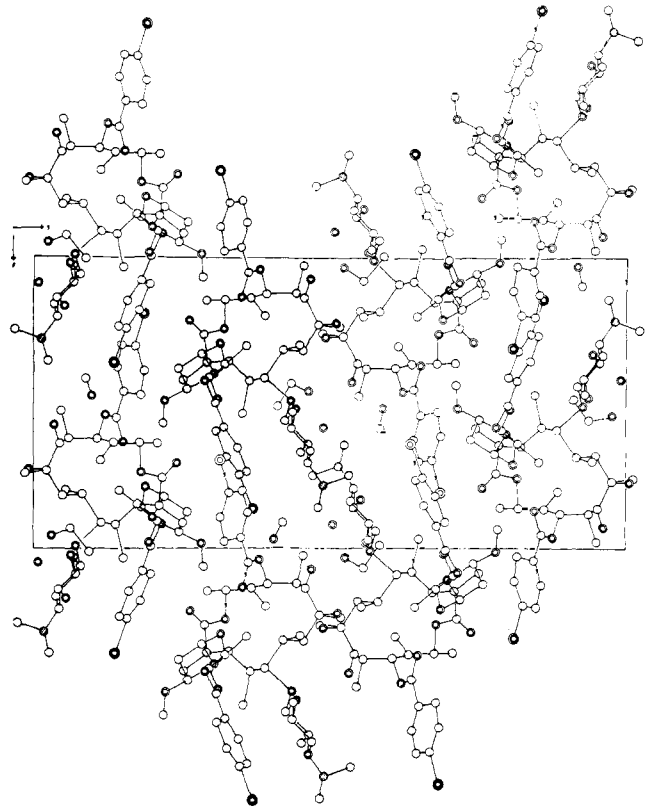


Figure 3. Packing cell of 11,4″-bis[O-(p-bromobenzoyl)]oleandomycin (**2**).

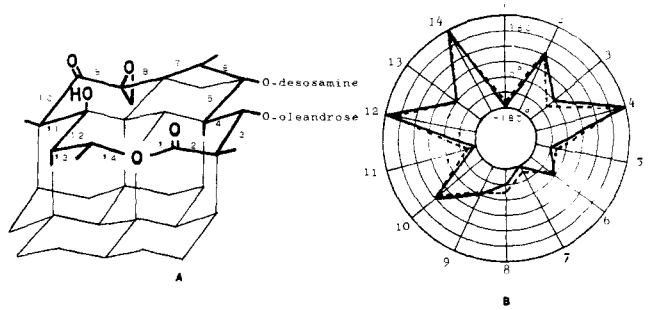


Figure 4. (A) Diamond model F applied to oleandomycin (**1**). (B) Maps of dihedral angles: from diamond model F (—); from X-ray (- - -).

accurately measured 2θ values of 24 strong reflections in the range of $16 \leq 2\theta \leq 30°$. The scan range of ω for each reflection was calculated by the formula $\omega = 1.10° + 0.5 \tan\theta$, and the background was measured at both ends of the scan range for 10.0 s.

Three standard reflections were measured after every 60 reflections. The maximum deviation of the standard from their mean values was 3.5%. A total of 3440 independent reflections with 2θ less than 150° were measured in the ω–2θ scanning mode (2°/min), and of these 2266 had $|F_o|$ values greater than three times their standard deviations and were used in the structure analysis.

Determination of the Structure

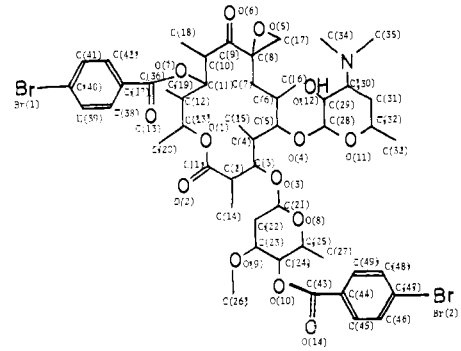
The structure was solved by the heavy-atom method. All the rest of 65 nonhydrogen atoms in the asymmetric unit were deduced. The oxygen atoms and nitrogen atom were assigned on the basis of the chemical consideration. An ethanol [C(50), C(51), and O(51)] and a methanol [C(52) and C(53)] were located in a molecule. One of these is oxygen, but refinement was performed as a carbon atom. Final least-squares refinements containing anisotropic temperature factors gave R = 0.112.[7] The atomic coordinates and thermal parameters with their estimated standard deviations are listed in Table I. Hydrogen atoms were not included in the refinement, and the absolute configuration was determined based on the absolute configuration of β-D-desosamine.[3,8,9] (See paragraph at end of paper regarding supplementary material.)

The structure of 11,4″-bis[O-(p-bromobenzoyl)]oleandomycin (**2**) is shown in Figure 2 which illustrates a c-axis projection of the molecule. The absolute configurations of the asymmetric centers are consistent with those established for oleandomycin (**1**). The chiral centers of the macrolactone ring are 2R,3S,4R,5S,6S,10R,11S,12R,13R. This conclusion is identical with that derived from the chemical degradation products.[2]

The bond lengths and bond angles of the molecule are shown in Tables II and III. Torsion angles of the lactone ring are listed in Table IV. The packing cell projected along the c axis is shown in Figure 3.

"Diamond Lattice" Conformation Model (Diamond Model). Celmer earlier proposed to apply Dale's "diamond lattice" conformation model[10] A (diamond model A) to 14-membered macrolide antibiotics.[11] Egan et al.[12] subsequently proposed an alternate "diamond lattice" conformation model B (diamond model B) to be applied to the 14-membered macrolac-

Table I. Final Least-Squares Parameters with Estimated Standard Deviations in Parentheses



atom	*x*	*y*	*z*	atom	*x*	*y*	*z*
Br(1)	−3019 (3)	3146 (1)	8450 (4)	C(35)	7436 (28)	5299 (9)	7629 (32)
Br(2)	8563 (3)	3631 (1)	13372 (4)	C(36)	535 (24)	3590 (10)	6073 (28)
C(1)	2663 (27)	2895 (10)	4833 (28)	C(37)	−341 (23)	3486 (8)	6615 (27)
C(2)	3675 (20)	2927 (9)	5223 (23)	C(38)	−1174 (19)	3640 (9)	6260 (21)
C(3)	3643 (27)	3252 (8)	6190 (25)	C(39)	−1988 (24)	3516 (10)	6758 (25)
C(4)	4258 (21)	3627 (9)	5954 (25)	C(40)	−1906 (25)	3285 (8)	7612 (28)
C(5)	4133 (23)	3952 (8)	6880 (25)	C(41)	−1050 (24)	3126 (12)	8081 (32)
C(6)	3177 (18)	4187 (7)	6781 (23)	C(42)	−282 (26)	3229 (11)	7543 (32)
C(7)	3192 (22)	4505 (8)	5861 (26)	C(43)	4898 (25)	3035 (11)	11411 (33)
C(8)	2323 (22)	4790 (8)	5821 (24)	C(44)	5772 (23)	3179 (9)	11932 (26)
C(9)	1373 (22)	4578 (8)	5593 (25)	C(45)	6461 (26)	3404 (9)	11281 (28)
C(10)	1204 (22)	4402 (8)	4466 (23)	C(46)	7338 (25)	3563 (10)	11747 (29)
C(11)	1267 (22)	3915 (8)	4644 (20)	C(47)	7450 (27)	3445 (10)	12785 (32)
C(12)	1270 (24)	3670 (9)	3579 (26)	C(48)	6826 (23)	3211 (9)	13399 (29)
C(13)	1410 (22)	3192 (9)	3867 (27)	C(49)	5966 (25)	3067 (12)	12962 (29)
C(14)	4113 (26)	2507 (10)	5431 (27)	N	7795 (18)	4868 (7)	7851 (22)
C(15)	5351 (23)	3493 (9)	5895 (26)	O(1)	2441 (15)	3187 (6)	4195 (16)
C(16)	3006 (24)	4415 (10)	7842 (25)	O(2)	2112 (17)	2610 (6)	5126 (21)
C(17)	2379 (28)	5239 (10)	5408 (31)	O(3)	3962 (13)	3034 (5)	7127 (14)
C(18)	327 (22)	4524 (9)	3943 (26)	O(4)	4870 (13)	4270 (5)	6805 (16)
C(19)	2028 (28)	3844 (10)	2811 (31)	O(5)	2299 (15)	5128 (5)	6504 (20)
C(20)	1395 (28)	2917 (11)	2902 (30)	O(6)	722 (17)	4609 (6)	6181 (18)
C(21)	3289 (24)	2832 (9)	7743 (25)	O(7)	453 (13)	3780 (5)	5176 (15)
C(22)	3732 (24)	2453 (9)	8333 (29)	O(8)	2947 (15)	3128 (6)	8521 (18)
C(23)	4456 (24)	2585 (9)	9078 (27)	O(9)	4795 (17)	2219 (7)	9613 (19)
C(24)	4079 (22)	2896 (9)	9849 (25)	O(10)	4817 (16)	3073 (7)	10410 (16)
C(25)	3643 (24)	3280 (9)	9301 (25)	O(11)	5172 (14)	4348 (5)	8574 (17)
C(26)	5682 (27)	2192 (12)	9890 (30)	O(12)	6698 (15)	4443 (6)	6221 (18)
C(27)	3014 (27)	3559 (10)	10122 (25)	O(13)	1312 (16)	3501 (7)	6477 (19)
C(28)	5566 (21)	4251 (9)	7611 (30)	O(14)	4238 (17)	2882 (8)	11995 (18)
C(29)	6322 (26)	4576 (10)	7203 (30)	C(50)	5003 (55)	4195 (21)	3450 (65)
C(30)	7062 (22)	4553 (8)	8042 (25)	C(51)	4163 (48)	4467 (21)	3013 (43)
C(31)	6597 (23)	4619 (10)	9190 (28)	C(52)	4050 (56)	842 (24)	9711 (68)
C(32)	5895 (19)	4281 (9)	9421 (24)	C(53)	4798 (55)	926 (24)	9802 (67)
C(33)	5329 (24)	4348 (10)	10375 (24)	O(15)	4656 (56)	4783 (20)	3544 (65)
C(34)	8545 (25)	4743 (11)	7093 (28)	O(16)	5999 (21)	4982 (11)	4644 (23)

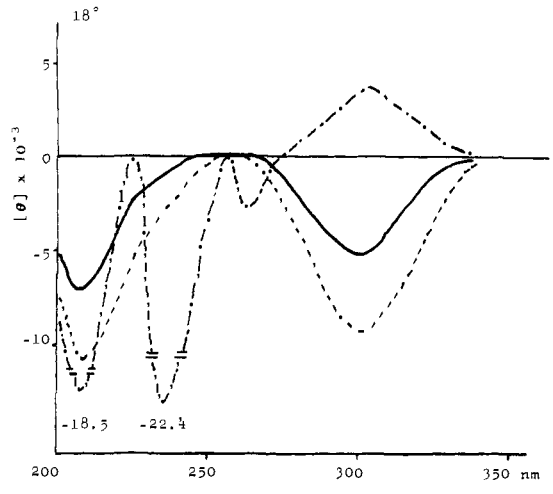


Figure 5. CD curves of **1** (—, MeOH; - - -, dioxane) and **2** (—·—, MeOH or dioxane).

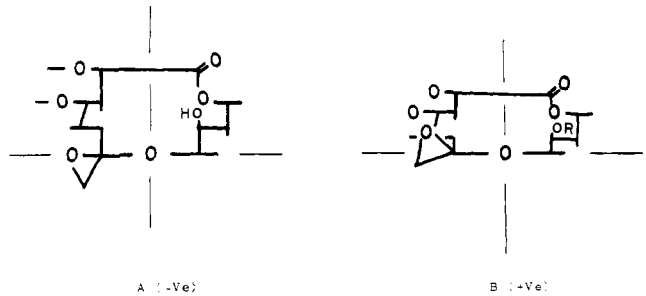


Figure 6. Octant projection of oleandomycin (A) and its benzoate (B).

tone of erythromycin antibiotics. In an earlier paper, we proposed the application of a "diamond lattice" conformation model C[13] (diamond model C) to the 14-membered macrolactone of kromycin. Very recently, based on the X-ray analysis, we proposed a new "diamond lattice" conformation model D[14] (diamond model D) for the 14-membered macrolactone

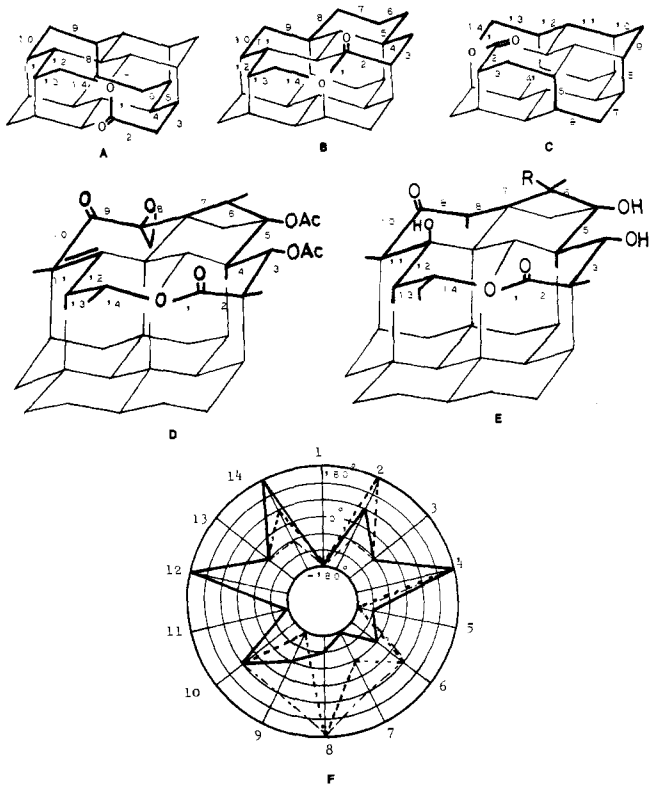


Figure 7. (A) Diamond model A. (B) Diamond model B. (C) Diamond model C. (D) Diamond model F applied to the diacetylanhydroaglycon (4) of oleandomycin. (E) Diamond model F applied to erythronolide B (R = OH) and 6-deoxyerythronolide B (R = H). (F) Maps of dihedral angles: from diamond model A (—·—); from diamond model B (- - -); from diamond model F (—).

Table II. Bond Lengths (Å)

Br(1)-C(40)	1.97 (36)	C(38)-C(39)	1.39 (44)
Br(2)-C(47)	1.86 (38)	C(39)-C(40)	1.32 (46)
C(1)-C(2)	1.54 (49)	C(40)-C(41)	1.46 (50)
C(1)-O(1)	1.28 (39)	C(41)-C(42)	1.34 (53)
C(1)-O(2)	1.27 (41)	O(3)-C(21)	1.41 (37)
C(2)-C(3)	1.62 (41)	C(21)-O(8)	1.46 (38)
C(2)-C(14)	1.51 (43)	C(21)-C(22)	1.57 (44)
C(3)-C(4)	1.53 (43)	O(8)-C(25)	1.49 (39)
C(3)-O(3)	1.46 (36)	C(27)-C(25)	1.59 (47)
C(4)-C(5)	1.58 (42)	C(24)-O(10)	1.40 (38)
C(4)-C(15)	1.59 (44)	C(24)-C(23)	1.50 (44)
C(5)-C(6)	1.57 (40)	C(24)-C(25)	1.55 (43)
C(5)-O(4)	1.48 (34)	O(14)-C(43)	1.29 (45)
C(6)-C(7)	1.56 (40)	O(10)-C(43)	1.28 (47)
C(6)-C(16)	1.56 (43)	C(23)-O(9)	1.45 (38)
C(7)-C(8)	1.55 (42)	C(23)-C(22)	1.47 (49)
C(8)-C(9)	1.55 (43)	O(9)-C(26)	1.32 (46)
C(8)-O(5)	1.39 (35)	C(30)-N	1.48 (38)
C(8)-C(17)	1.54 (44)	C(30)-C(31)	1.58 (47)
C(9)-C(10)	1.56 (42)	C(30)-C(29)	1.51 (49)
C(9)-O(6)	1.20 (39)	N-C(34)	1.50 (45)
C(10)-C(11)	1.59 (38)	N-C(35)	1.51 (39)
C(10)-C(18)	1.48 (45)	O(11)-C(32)	1.51 (36)
C(11)-C(12)	1.57 (42)	O(11)-C(28)	1.39 (42)
C(11)-O(7)	1.42 (35)	C(32)-C(35)	1.48 (43)
C(12)-C(13)	1.59 (41)	C(32)-C(31)	1.51 (43)
C(12)-C(19)	1.57 (51)	C(29)-O(12)	1.42 (44)
C(13)-C(14)	1.54 (38)	C(29)-C(28)	1.57 (47)
C(13)-C(20)	1.52 (50)	C(47)-C(48)	1.41 (50)
O(4)-C(43)	1.44 (40)	C(47)-C(46)	1.39 (54)
O(5)-C(17)	1.45 (47)	C(48)-C(49)	1.43 (49)
O(7)-C(36)	1.30 (40)	C(45)-C(44)	1.48 (47)
C(36)-O(13)	1.26 (41)	C(45)-C(46)	1.48 (50)
C(36)-C(37)	1.47 (47)	C(44)-C(49)	1.39 (50)
C(37)-C(38)	1.37 (42)	C(44)-C(43)	1.50 (50)
C(37)-C(42)	1.45 (51)		

Table III. Bond Angles (deg)

C(2)-C(1)-O(1)	113 (28)	C(41)-C(40)-C(39)	128 (32)
C(2)-C(1)-O(2)	123 (30)	Br(1)-C(40)-C(39)	120 (25)
O(1)-C(1)-O(2)	124 (31)	C(42)-C(41)-C(40)	113 (33)
C(3)-C(2)-C(1)	105 (24)	C(21)-O(3)-C(3)	118 (22)
C(3)-C(2)-C(14)	117 (25)	O(8)-C(21)-O(3)	108 (23)
C(1)-C(2)-C(14)	113 (26)	O(8)-C(21)-C(22)	108 (24)
C(4)-C(3)-C(2)	110 (25)	O(3)-C(21)-C(22)	110 (25)
C(4)-C(3)-O(3)	111 (25)	C(25)-O(8)-C(21)	116 (22)
C(2)-C(3)-O(3)	108 (23)	O(10)-C(24)-C(23)	110 (25)
C(5)-C(4)-C(3)	108 (24)	O(10)-C(24)-C(25)	102 (24)
C(5)-C(4)-C(15)	109 (23)	C(23)-C(24)-C(25)	113 (26)
C(3)-C(4)-C(15)	111 (25)	C(43)-O(10)-C(24)	122 (27)
C(6)-C(5)-C(4)	111 (23)	O(9)-C(23)-C(24)	111 (26)
C(6)-C(5)-O(4)	107 (22)	O(9)-C(23)-C(22)	108 (26)
C(4)-C(5)-O(4)	109 (22)	C(24)-C(23)-C(22)	111 (27)
C(7)-C(6)-C(5)	111 (22)	C(26)-O(9)-C(23)	120 (27)
C(7)-C(6)-C(16)	110 (23)	N-C(30)-C(31)	111 (24)
C(5)-C(6)-C(16)	107 (22)	N-C(30)-C(29)	110 (25)
C(8)-C(7)-C(6)	114 (24)	C(31)-C(30)-C(29)	110 (25)
C(9)-C(8)-C(7)	117 (24)	C(34)-N-C(30)	116 (25)
C(9)-C(8)-O(5)	116 (24)	C(34)-N-C(35)	112 (26)
C(9)-C(8)-C(17)	113 (26)	C(30)-N-C(35)	115 (25)
C(7)-C(8)-O(5)	118 (24)	C(32)-O(11)-C(28)	109 (21)
C(7)-C(8)-C(17)	122 (26)	C(33)-C(32)-O(11)	101 (22)
O(5)-C(8)-C(17)	59 (26)	C(33)-C(32)-C(31)	115 (26)
C(10)-C(9)-C(8)	118 (24)	O(11)-C(32)-C(31)	103 (22)
C(10)-C(9)-O(6)	119 (26)	O(12)-C(29)-C(30)	110 (27)
C(8)-C(9)-O(6)	122 (27)	O(12)-C(29)-C(28)	110 (27)
C(11)-C(10)-C(9)	103 (22)	C(30)-C(29)-C(28)	102 (26)
C(11)-C(10)-C(18)	112 (24)	C(48)-C(47)-Br(2)	120 (27)
C(9)-C(10)-C(18)	117 (25)	C(48)-C(47)-C(46)	127 (34)
C(12)-C(11)-C(10)	112 (23)	Br(2)-C(47)-C(46)	113 (27)
C(12)-C(11)-O(7)	105 (22)	C(49)-C(48)-C(47)	120 (32)
C(10)-C(11)-O(7)	109 (22)	C(44)-C(45)-C(46)	121 (29)
C(13)-C(12)-C(11)	107 (24)	C(49)-C(44)-C(45)	121 (30)
C(13)-C(12)-C(19)	114 (27)	C(49)-C(44)-C(43)	121 (30)
C(11)-C(12)-C(19)	111 (26)	C(45)-C(44)-C(43)	118 (29)
O(1)-C(13)-C(12)	101 (23)	C(1)-O(1)-C(13)	115 (24)
O(1)-C(13)-C(20)	103 (25)	C(8)-C(17)-O(5)	56 (20)
C(12)-C(13)-C(20)	112 (27)	O(4)-C(28)-O(11)	110 (24)
C(28)-O(4)-C(5)	115 (21)	O(4)-C(28)-C(29)	102 (24)
C(16)-C(15)-C(8)	66 (22)	O(11)-C(28)-C(29)	115 (26)
C(20)-O(7)-C(11)	119 (23)	C(32)-C(42)-C(41)	121 (34)
O(13)-C(36)-O(7)	123 (30)	C(21)-C(22)-C(23)	112 (27)
O(13)-C(36)-C(37)	121 (30)	O(8)-C(25)-C(27)	104 (23)
O(7)-C(36)-C(37)	116 (28)	O(8)-C(25)-C(24)	108 (24)
C(38)-C(37)-C(36)	121 (28)	C(27)-C(25)-C(24)	112 (25)
C(38)-C(37)-C(41)	122 (29)	O(14)-C(43)-O(10)	123 (33)
C(36)-C(37)-C(41)	118 (29)	O(14)-C(43)-C(44)	118 (31)
C(29)-C(28)-C(37)	119 (27)	O(10)-C(43)-C(44)	119 (31)
C(40)-C(39)-C(38)	118 (30)	C(30)-C(31)-C(32)	111 (25)
C(41)-C(40)-Br(1)	112 (24)	C(47)-C(46)-C(45)	113 (31)
		C(48)-C(49)-C(44)	117 (32)

Table IV. Torsion Angles of Lactone Ring (deg)

C(2)-C(1)-O(1)-C(13)	−174
C(3)-C(2)-C(1)-O(1)	84
C(4)-C(3)-C(2)-C(1)	−119
C(5)-C(4)-C(3)-C(2)	175
C(6)-C(5)-C(4)-C(3)	−76
C(7)-C(6)-C(5)-C(4)	−73
C(8)-C(7)-C(6)-C(5)	−172
C(9)-C(8)-C(7)-C(6)	−65
C(10)-C(9)-C(8)-C(7)	−70
C(11)-C(10)-C(9)-C(8)	107
C(12)-C(11)-C(10)-C(9)	−171
C(13)-C(12)-C(11)-C(10)	176
O(1)-C(13)-C(12)-C(11)	−73
C(1)-O(1)-C(13)-C(12)	154

Table V. ^{13}C NMR Data of Oleandomycins ($CDCl_3$; δ, ppm)

compd	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13	C-14	2-Me	4-Me	6-Me	8-CH_2	10-Me	12-Me
1	176.3	44.9	81.4	30.5	84.1	30.5	44.9	62.6	208.0	43.2	70.3	41.9	69.3	14.8	18.5	9.0	20.1	48.9	5.9	9.6
2	175.0	44.1	78.4	32.8	84.3	33.2	44.1	62.7	207.0	42.8	73.5	40.6	69.1	12.7	19.2	11.7	18.4	51.0	10.9	10.6
3	175.1	44.2	79.0	33.5	84.3	32.2	44.2	63.2	207.4	42.6	71.7	40.0	69.1	13.1	18.8	10.9	17.7	51.0	10.2	10.2

	oleandrose							desosamine								benzoate	
compd	C-1′	C-2′	C-3′	C-4′	C-5′	C-6′	O-Me	C-1″	C-2″	C-3″	C-4″	C-5″	C-6″	C-7″	C-8″	ketone	aromatic carbon
1	99.8	34.0	78.0	76.1	68.8	17.9	56.4	104.5	70.6	65.6	28.6	69.3	21.3	40.3	40.3		
2	98.7	34.7	78.3	77.0	67.1	17.7	56.6	102.1	72.3	63.7	30.8	70.7	21.0	40.6	40.6	165.0, 164.7	131.6, 127.9
3	99.0	34.6	75.7	76.1	67.1	17.7	56.5	102.2	71.9	63.7	30.5	70.3	21.5	40.7	40.7		

of *p*-bromobenzoylpikromycin.

Now in this paper, we propose the most favorable and new "diamond lattice" conformation model F (diamond model F) (Figure 4) for the 14-membered macrolactone of oleandomycin on the basis of the torsion angles of **2** (Table IV). It is clear that diamond model F fits the conformation of **2**, and this is proved by the maps of dihedral angles shown in Figure 4. Evidently, the shape and each dihedral angle determined by X-ray analysis (dotted line) are in accord with those estimated from diamond model F (solid line). This diamond model F is constructed from three chair cyclohexane and one boat cyclohexane at C(5)–C(6)–C(7) as shown in Figure 4. This conformation fits the partially eclipsed conformation after Egan et al.[16] and Nourse and Roberts[17] for erythromycin derivatives.

As seen from diamond model F, the carbonyl group at the 9 position and the hydroxyl group at the 11 position are very near to each other, and it suggests the intramolecular hydrogen bond formation. This was proved from IR data in 0.001 M carbon tetrachloride solution ($\nu_{C=O}$ for **1**, 1692 cm^{-1}; for **2** and **3**, 1720 cm^{-1}). CD curves of **1** and **2** in methanol and dioxane are shown in Figure 5. Attention should be paid to the reversal of the sign of the n–π^* Cotton effect owing to the carbonyl group at the 9 position which appeared around 300 nm.[15]

Octant projection (A) of **1** predicts a negative Cotton effect owing to the ethylene oxide group which is caused by the intramolecular hydrogen bonding between the carbonyl group and hydroxyl group. When the hydroxyl group at the 11 position was acetylated or benzoylated (**2** or **3**), the hydrogen bond is broken and a conformational moving causes a positive Cotton effect (B) as shown in Figure 6. This conformation (B) agrees with the one resulting from the X-ray analysis. Similar conformational moving was reported in erythronolide B and it derivatives based on the NMR and CD studies.[16-18] This conclusion is further supported by the ^{13}C NMR spectra[17] (Table V).

Application of diamond model F to the diacetylanhydroaglycon (**4**) of oleandomycin is shown in Figure 7. The NMR coupling constants of **4** are probable to this conformation.

In conclusion, diamond model F is in accordance with the conformation of oleandomycin and erythromycin derivatives (Figure 7) rather than diamond models A or B. This is clearly proved by the maps of dihedral angles for diamond model F (solid line) and diamond model B (dotted line) shown in Figure 7.

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Supplementary Material Available: Listings of the observed and final thermal parameters (9 pages). Ordering information is given on any current masthead page.

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