256. The Structure of the Antibiotic Hedamycin. V. Crystal Structure and Absolute Configuration[1])

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Summary

The crystal structure of the antibiotic hedamycin (**1**) has been solved by direct method and refined by least squares techniques to $R=0.091$ for 2289 of 2643 independent reflexions. Crystals of $C_{41}H_{50}N_2O_{11}$ are orthorhombic, space group $P2_12_12_1$ with lattice parameters $a=24.239$ (12), $b=21.440$ (10), $c=7.369$ (4) Å, $Z=4$. The structural features of hedamycin derived earlier by chemical and spectroscopical means are confirmed. Optical rotation and circular dichroism indicate that hedamycin (**1**) has the absolute configuration of the related antibiotic kidamycin (**3**). The conformation of ring F is a chair form with the aryl substituent almost axial. The bioxirane part of the antibiotic is in a synclinal conformation.

Introduction. – The structure of the antitumor antibiotic hedamycin (**1**) has recently been elucidated by chemical and spectroscopic means (*cf.* [1] and ref. therein). The relative configurations in the two tetrahydropyran rings E and F on the one hand, and in the diepoxide side chain on the other hand were also determined. It was not possible, however, to derive the relative configuration of the side chain with respect to rings E and F, nor to determine the absolute configuration of the whole molecule.

A crystal structure analysis seemed to be the best means to fill these gaps and yield additional insight into conformational aspects of hedamycin and related compounds. We were not able to prepare a suitable heavy atom derivative, but hedamycin itself could be crystallized from chloroform/heptane in a form suitable for X-ray structure determination.

Results and discussion. – The X-ray structure determination revealed the molecular structure shown in *Figure 1* (the figure does not give the absolute configuration). Structural features that had been determined by chemical and spectroscopic means [2] [3] are confirmed, including the unique diepoxide side chain and the relative configurations within this particular fragment [1].

[1]) Presented in part at the fall meeting of the Swiss Chemical Society in Bern, October 19, 1979. Part IV: [1].

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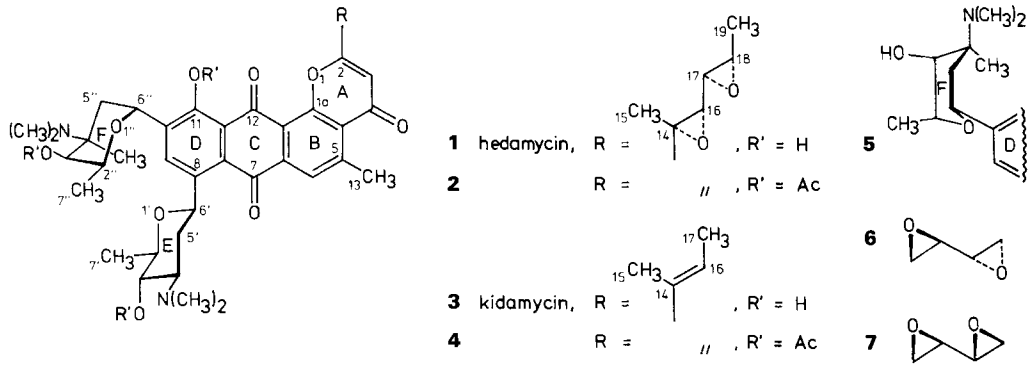

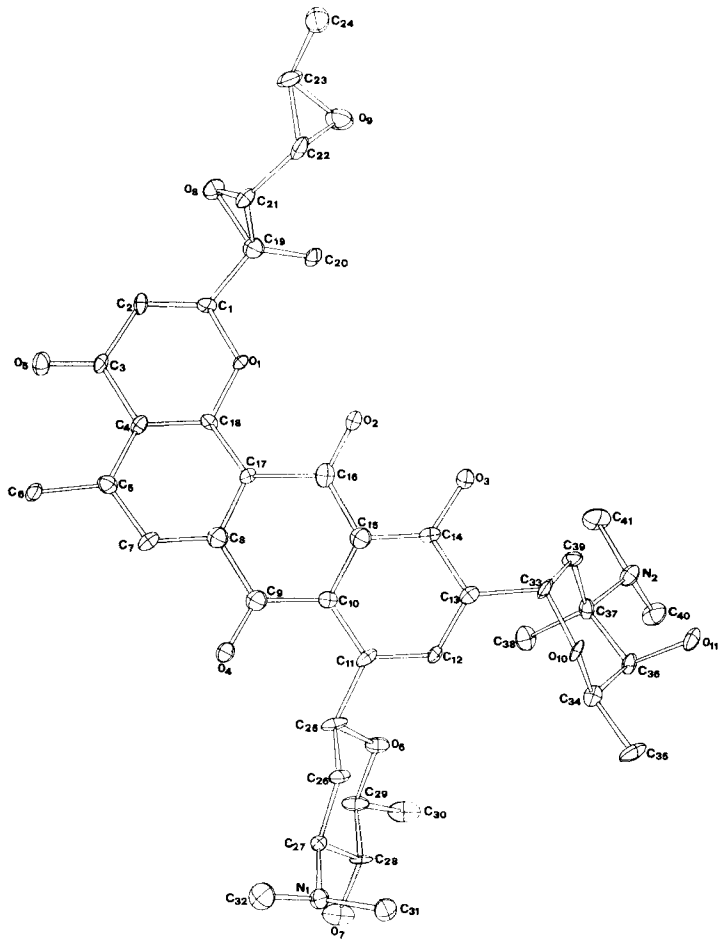

Fig. 1. *ORTEP plot of the hedamycin molecule.* This figure does **not** define the absolute configuration.

Table 1. *Optical rotations of hedamycin, kidamycin and their triacetates*

Compound	mw	$[\alpha]_D$	$[\Phi]_D$	$\Delta[\Phi]_D = [\Phi]_{acetate} - [\Phi]_{parent\ compound}$
Kidamycin (**3**)	689	+476° [4]	+3279°	−1191°
Tri-*O*-acetylkidamycin (**4**)	815	+256° [4]	+2088°	
Hedamycin (**1**)	747	+406°	+3032°	−1749°
Tri-*O*-acetylhedamycin (**2**)	873	+147°	+1283°	

Since diffractions were not made on a heavy atom derivative, no information about the absolute configuration could be obtained. However, a first indication that hedamycin might have the same absolute configuration as the closely related antibiotic kidamycin (**3**) [4] came from a comparison of the optical rotations of the two antibiotics and their tri-*O*-acetyl derivatives **2** and **4** *(cf. Table 1)*. If one assumes the diepoxide side chain in hedamycin is remote enough from the tetrahydropyran rings for *Freudenberg's* principle of optical superposition [5] to hold, and further that the increment of the side chain to the total optical rotation of hedamycin is not affected by acetylation, one would expect similar increments in molecular rotations $\Delta[\Phi]$ upon acetylation of hedamycin and kidamycin if their absolute configurations were the same. Opposite increments, however, should be observed if the two antibiotics had opposite absolute configurations. Since the observed increments $\Delta[\Phi]$ are both negative and of comparable magnitudes *(cf. Table 1)* hedamycin (**1**) must have the same absolute configuration as kidamycin (**3**). This result is further corroborated by the close resemblence of the CD. curves of the two antibiotics *(Fig. 2)*. Thus the absolute configuration of hedamycin is (14*R*, 16*S*, 17*R*, 18*S*, 2′*R*, 3′*S*, 4′*R*, 6′*R*, 2″*S*, 3″*S*, 4″*S*, 6″*R*), as shown in formula **1**.

The crystal structure also reveals interesting details of the conformation hedamycin adopts in the crystal. The conformation of ring F is of particular interest. An X-ray study of a kidamycin derivative having the two dimethylamino groups quaternized with methyl iodide, showed ring F in a non-chair conformation [4] [6]. Thereafter, kidamycins, hedamycins and pluramycins were represented as in formula **5** with ring F as a boat or twisted boat form, even when the amino groups were not quaternized. NMR. measurements of $^1H, ^1H$-coupling constants and ^{13}C-acetylation shifts seemed to point to a flexible non-chair conformation for ring F also in solution [3]. The basic assumption of that discussion was that the large aryl group should be in an equatorial or pseudoequatorial position. *Figure 1* indicates that in hedamycin crystals ring F is surprisingly in a chair conformation with the aryl group *axial*. It can clearly be seen, however, that the orientation is not truly axial, but rather bent outwards to relieve strain. Consequently, the ring is somewhat flattened with the endocyclic bond angles at C(5″), C(6″) and O(1″) opened up as compared with the corresponding angles in ring E *(cf. Table 4)*. Hedamycins and related compounds are thus more accurately represented by formula **1** than by formula **5**. Our findings demonstrate the advantage of measuring the parent compound rather than a heavy atom derivative, since the conformation found by study of a heavy atom derivative is not necessarily representative of the

Table 2. *Positional and thermal parameters of the non-hydrogen atoms and their standard deviations.* The temperature factors are of the form $T = \exp\{-2\pi^2(U_{11}h^2a^{*2} + \ldots + 2U_{12}hka^*b^*)\}$

Atom[a])	x	y	z	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.3366 (4)	−0.0612 (5)	1.4878 (13)	0.0218 (5)	0.0202 (5)	0.0091 (5)	0.0045 (4)	−0.0062 (4)	−0.0028 (4)
C(2)	0.3074 (4)	−0.0333 (5)	1.6225 (14)	0.0171 (4)	0.0323 (5)	0.0167 (5)	−0.0013 (4)	0.0050 (4)	0.0034 (4)
C(3)	0.2913 (4)	0.0330 (5)	1.6137 (14)	0.0303 (5)	0.0198 (5)	0.0081 (5)	−0.0044 (4)	−0.0058 (5)	−0.0082 (4)
C(4)	0.3068 (4)	0.0650 (5)	1.4372 (14)	0.0182 (5)	0.0306 (3)	0.0157 (5)	0.0031 (4)	−0.0042 (4)	−0.0056 (4)
C(5)	0.2903 (5)	0.1270 (5)	1.4001 (16)	0.0282 (5)	0.0298 (5)	0.0219 (5)	0.0038 (5)	−0.0021 (5)	0.0069 (5)
C(6)	0.2533 (5)	0.1646 (5)	1.5227 (16)	0.0323 (5)	0.0372 (5)	0.0296 (5)	0.0020 (5)	0.0150 (5)	0.0074 (5)
C(7)	0.3082 (4)	0.1553 (5)	1.2359 (14)	0.0312 (5)	0.0327 (5)	0.0055 (5)	−0.0046 (5)	−0.0068 (4)	0.0028 (5)
C(8)	0.3410 (5)	0.1215 (5)	1.1125 (14)	0.0310 (5)	0.0272 (5)	0.0143 (5)	−0.0047 (5)	−0.0025 (5)	−0.0070 (4)
C(9)	0.3587 (4)	0.1549 (4)	0.9421 (13)	0.0160 (4)	0.0128 (4)	0.0150 (5)	−0.0086 (4)	−0.0010 (4)	0.0051 (4)
C(10)	0.3976 (4)	0.1250 (5)	0.8158 (13)	0.0088 (4)	0.0177 (5)	0.0164 (5)	0.0005 (4)	−0.0068 (4)	0.0022 (4)
C(11)	0.4241 (4)	0.1564 (5)	0.6719 (15)	0.0231 (5)	0.0316 (5)	0.0196 (5)	0.0087 (5)	0.0010 (5)	−0.0059 (5)
C(12)	0.4525 (4)	0.1227 (5)	0.5435 (14)	0.0291 (5)	0.0267 (5)	0.0077 (5)	−0.0026 (4)	−0.0029 (4)	−0.0041 (4)
C(13)	0.4606 (4)	0.0592 (5)	0.5537 (14)	0.0154 (5)	0.0278 (5)	0.0209 (5)	0.0025 (5)	0.0033 (5)	−0.0048 (4)
C(14)	0.4384 (4)	0.0268 (5)	0.7094 (14)	0.0274 (5)	0.0220 (5)	0.0122 (5)	0.0061 (4)	−0.0140 (4)	−0.0010 (4)
C(15)	0.4066 (4)	0.0603 (5)	0.8357 (12)	0.0230 (5)	0.0271 (5)	0.0038 (4)	−0.0024 (4)	0.0052 (4)	−0.0040 (4)
C(16)	0.3853 (4)	0.0234 (5)	0.9931 (16)	0.0221 (5)	0.0279 (5)	0.0279 (5)	−0.0022 (5)	−0.0095 (5)	−0.0021 (5)
C(17)	0.3550 (4)	0.0586 (5)	1.1459 (13)	0.0185 (5)	0.0213 (5)	0.0064 (5)	−0.0056 (4)	−0.0012 (4)	−0.0069 (4)
C(18)	0.3383 (4)	0.0324 (5)	1.3050 (13)	0.0314 (5)	0.0120 (5)	0.0121 (5)	0.0019 (4)	−0.0060 (4)	0.0038 (4)
C(19)	0.3532 (4)	−0.1292 (5)	1.4777 (14)	0.0314 (5)	0.0254 (5)	0.0081 (5)	0.0003 (5)	−0.0058 (5)	−0.0048 (5)
C(20)	0.4113 (4)	−0.1436 (5)	1.4140 (15)	0.0345 (5)	0.0220 (5)	0.0248 (5)	0.0026 (5)	0.0020 (5)	0.0069 (5)
C(21)	0.3053 (5)	−0.1733 (6)	1.4717 (15)	0.0306 (5)	0.0481 (5)	0.0165 (5)	−0.0024 (5)	−0.0053 (5)	−0.0083 (5)
C(22)	0.3088 (4)	−0.2398 (5)	1.4012 (16)	0.0241 (5)	0.0402 (5)	0.0316 (5)	−0.0043 (5)	0.0054 (5)	0.0008 (5)
C(23)	0.3060 (5)	−0.2922 (6)	1.5300 (18)	0.0465 (5)	0.0372 (5)	0.0389 (6)	0.0121 (5)	0.0150 (5)	−0.0055 (5)
C(24)	0.2800 (6)	−0.3546 (6)	1.4851 (20)	0.0526 (6)	0.0427 (6)	0.0719 (6)	−0.0071 (6)	0.0273 (6)	−0.0116 (6)
C(25)	0.4269 (4)	0.2294 (5)	0.6623 (15)	0.0230 (5)	0.0377 (5)	0.0225 (5)	0.0122 (5)	−0.0133 (5)	−0.0110 (5)
C(26)	0.3926 (4)	0.2583 (5)	0.5120 (16)	0.0264 (5)	0.0194 (5)	0.0318 (5)	0.0028 (5)	0.0030 (5)	−0.0064 (4)
C(27)	0.4082 (4)	0.3289 (5)	0.4924 (14)	0.0272 (5)	0.0223 (5)	0.0173 (5)	0.0070 (5)	0.0041 (5)	0.0029 (4)

Atom[a])	x	y	z	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(28)	0.4699 (4)	0.3363 (4)	0.4586 (14)	0.0237 (5)	0.0140 (5)	0.0269 (5)	0.0071 (5)	−0.0147 (4)	−0.0088 (4)
C(29)	0.5027 (5)	0.3034 (5)	0.6183 (17)	0.0290 (5)	0.0295 (5)	0.0335 (5)	0.0117 (5)	−0.0091 (5)	−0.0145 (5)
C(30)	0.5644 (5)	0.3013 (6)	0.5820 (18)	0.0300 (5)	0.0422 (5)	0.0526 (6)	0.0051 (6)	−0.0265 (5)	−0.0099 (5)
C(31)	0.3789 (5)	0.3347 (6)	0.1679 (16)	0.0333 (5)	0.0454 (5)	0.0203 (5)	−0.0012 (5)	−0.0008 (5)	0.0064 (5)
C(32)	0.3155 (5)	0.3734 (6)	0.4033 (19)	0.0430 (6)	0.0540 (6)	0.0402 (6)	−0.0035 (6)	−0.0012 (6)	0.0068 (6)
C(33)	0.4912 (5)	0.0198 (5)	0.4114 (15)	0.0406 (5)	0.0303 (5)	0.0123 (5)	0.0010 (5)	0.0007 (5)	−0.0033 (5)
C(34)	0.5423 (5)	0.0910 (5)	0.2052 (15)	0.0251 (5)	0.0345 (5)	0.0196 (5)	−0.0096 (5)	−0.0046 (5)	−0.0012 (5)
C(35)	0.5377 (5)	0.1134 (6)	0.0109 (16)	0.0528 (6)	0.0429 (6)	0.0125 (5)	0.0017 (5)	−0.0045 (5)	−0.0143 (5)
C(36)	0.5955 (4)	0.0563 (5)	0.2448 (14)	0.0191 (5)	0.0373 (5)	0.0169 (5)	−0.0064 (5)	−0.0026 (5)	0.0026 (5)
C(37)	0.5984 (4)	0.0360 (5)	0.4480 (14)	0.0228 (5)	0.0303 (5)	0.0206 (5)	0.0033 (4)	0.0042 (4)	0.0109 (4)
C(38)	0.6014 (5)	0.0939 (5)	0.5757 (16)	0.0334 (5)	0.0412 (5)	0.0266 (5)	−0.0130 (5)	−0.0080 (5)	0.0052 (5)
C(39)	0.5473 (4)	−0.0065 (5)	0.4785 (15)	0.0199 (5)	0.0296 (5)	0.0270 (5)	0.0090 (5)	0.0010 (4)	0.0059 (4)
C(40)	0.7020 (5)	0.0232 (6)	0.4198 (19)	0.0248 (6)	0.0557 (6)	0.0551 (6)	0.0052 (6)	0.0130 (5)	0.0003 (5)
C(41)	0.6533 (6)	−0.0356 (6)	0.6509 (17)	0.0610 (6)	0.0513 (6)	0.0303 (6)	0.0072 (6)	−0.0220 (6)	0.0009 (6)
N(1)	0.3770 (4)	0.3629 (4)	0.3547 (13)	0.0354 (5)	0.0297 (5)	0.0288 (5)	−0.0020 (4)	−0.0042 (4)	−0.0008 (4)
N(2)	0.6487 (3)	−0.0067 (4)	0.4657 (11)	0.0269 (4)	0.0364 (4)	0.0176 (4)	−0.0085 (4)	0.0010 (4)	−0.0044 (4)
O(1)	0.3530 (3)	−0.0298 (3)	1.3355 (9)	0.0277 (3)	0.0221 (3)	0.0085 (3)	0.0040 (3)	0.0075 (3)	0.0045 (3)
O(2)	0.3921 (3)	−0.0342 (3)	1.0071 (10)	0.0440 (4)	0.0257 (4)	0.0204 (4)	−0.0007 (3)	0.0077 (3)	−0.0002 (3)
O(3)	0.4494 (3)	−0.0349 (3)	0.7201 (10)	0.0291 (4)	0.0299 (4)	0.0201 (4)	0.0008 (3)	0.0044 (3)	−0.0020 (3)
O(4)	0.3383 (3)	0.2075 (3)	0.9078 (10)	0.0375 (4)	0.0290 (4)	0.0215 (4)	−0.0013 (4)	−0.0007 (4)	0.0029 (3)
O(5)	0.2698 (3)	0.0604 (4)	1.7392 (10)	0.0320 (4)	0.0423 (4)	0.0166 (4)	−0.0031 (3)	0.0066 (4)	0.0128 (3)
O(6)	0.4865 (3)	0.2375 (3)	0.6217 (10)	0.0305 (4)	0.0219 (4)	0.0261 (4)	0.0018 (3)	0.0012 (3)	−0.0058 (3)
O(7)	0.4847 (4)	0.4006 (4)	0.4683 (13)	0.0678 (5)	0.0315 (4)	0.0553 (5)	0.0095 (4)	−0.0257 (5)	−0.0178 (4)
O(8)	0.3333 (3)	−0.1603 (4)	1.6406 (10)	0.0350 (4)	0.0392 (4)	0.0143 (4)	0.0042 (4)	−0.0045 (4)	−0.0069 (4)
O(9)	0.3559 (3)	−0.2767 (4)	1.4323 (13)	0.0400 (4)	0.0299 (4)	0.0590 (5)	0.0129 (4)	−0.0043 (4)	0.0030 (4)
O(10)	0.4940 (3)	0.0527 (3)	0.2399 (10)	0.0204 (4)	0.0300 (4)	0.0161 (4)	0.0013 (3)	−0.0027 (3)	0.0021 (3)
O(11)	0.6015 (3)	0.0042 (3)	0.1225 (10)	0.0373 (4)	0.0383 (4)	0.0190 (4)	−0.0030 (3)	0.0004 (3)	−0.0008 (3)

[a]) The numbering is that of *Figure 1.*

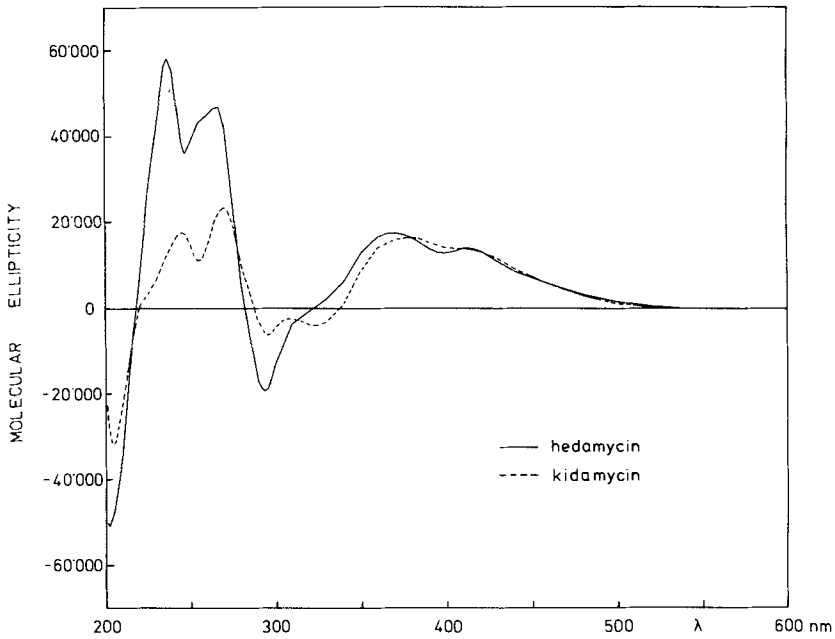

Fig. 2. *CD. curves of hedamycin* (**1**) *and kidamycin* (**3**) *in absolute ethanol*

conformation of the parent compound. The dihedral angles between the protons of ring F were calculated from the atomic coordinates. They are 63° between H–C(2″) and H–C(3″) and 41° and 77° between H–C(6″) and the two H–C(5″). The corresponding ^{1}H, ^{1}H-coupling constants calculated from the *Karplus* equation [7] would be 1, 5 and 0 Hz. These values, when compared with the experimental data of 3, 7 and 5 Hz [8], indicate that the conformation of hedamycin in solution is hardly the one the molecule displays in the crystal. Thus, despite the astounding crystal conformation found, we believe that our earlier discussion of the conformation of ring F in solution [3], which pointed rather to a flexible twist form, is still valid.

The present X-ray study also gives information about the solid state conformation of a substituted bioxirane. Whereas the crystal structure of bicyclopropyl was determined by *Eraker et al.* some years ago [9], no bioxirane derivative has ever been X-rayed to our knowledge. In bicyclopropyl the bond between the three-membered rings was 1.487 (4) Å, which is shorter than a normal single bond. This was interpreted in terms of conjugation between the rings. In contrast, the corresponding bond in hedamycin (1.507 (17) Å) is not significantly shorter than a normal C,C-bond. Furthermore, bicyclopropyl was shown to be in an antiperiplanar conformation in the crystal. The solid state conformation of bioxiranes was examined by *Lüttke & de Meijere* by IR. and *Raman* spectroscopy [10]. Their measurements indicated that the *meso*-form **6** was in a antiperiplanar conformation, whereas for the chiral isomer **7** and its enantiomer no conclusion could be drawn from the spectral data. Our experiments show that the diepoxide side chain of

hedamycin, which is a derivative of the chiral bioxirane **7**, is in a synclinal conformation with dihedral angles of 33° between the two O-atoms and 108° between C(14) and C(18). In this arrangement, each of the two epoxide oxygen atoms lies right above the plane of the other oxirane ring.

We thank Dr. *W. T. Bradner*, Syracuse, and Dr. *M. Furukawa*, Tokyo, for samples of hedamycin and kidamycin, respectively. The CD. spectra were kindly measured by Dr. *P. Moser* and *K. Jäkel* of *Ciba-Geigy AG*, Basel. We thank Prof. *U. Thewalt*, Ulm University, for allowing us to use the diffractometer, and the Universitätsrechenzentrum (URZ), Basel, for careful operating. Financial support by the *Swiss National Science Foundation* (project 2.624-0.76/2.122-0.78) and the *CIBA Foundation* is gratefully acknowledged.

Experimental Part

General remarks. Spectra were measured by *K. Aegerter* in the spectral laboratory of the *Institut für Organische Chemie* on the following instruments: UV. *Beckman* DK 2; IR. *Perkin-Elmer* 125; ^{1}H- and ^{13}C-NMR. *Bruker* WH 90. Optical rotations were determined on a *Perkin-Elmer* polarimeter 141. Elemental analyses were carried out by *E. Thommen* of the *Institut für Organische Chemie*. CD. spectra were recorded by Dr. *P. Moser* and *K. Jäkel* (*Ciba-Geigy AG*, Basel) on a *Jasco* J-20 spectropolarimeter.

Hedamycin (**1**) was a gift of Dr. *W. T. Bradner*, Bristol Laboratories, Syracuse, NY. $[\alpha]_D^{23} = +406° \pm 2°$ ($c = 0.1$, $CHCl_3$). – Spectral data: [2] [3]. – CD. (1.10M in abs. ethanol, *cf. Fig. 2*): 202 (−50900), 237 (+58100), 247 (+36000), 267 (+46900), 294 (−19300), 370 (+17400), 399 (+12800), 410 (+14000).

Crystals for X-ray structure determination: The open test tube containing hedamycin dissolved in a small amount of $CHCl_3$ was kept at RT. and in the dark in a sealed jar containing some heptane. After about 2 weeks an amorphous, resinous deposit of hedamycin had formed on the bottom of the test tube, from which relatively large crystals had grown. These were collected and their density determined by flotation in cyclohexane/1,3-dibromopropane.

11,3′,3″-Tri-O-acetylhedamycin (**2**). Hedamycin (101 mg) was dissolved in pyridine (40 µl). After the addition of acetic anhydride (400 µl), the reaction mixture was heated to 40° for 5 min and then left at 23° in a sealed tube in the dark for 3 days. Then, 10 ml of ice cold 10% aqueous $NaHCO_3$ were added and the mixture extracted with $CHCl_3$ (4×25 ml). The combined $CHCl_3$ extracts were washed with 60 ml of water, dried (Na_2SO_4), filtered and evaporated. The residue was dried *in vacuo* to yield 115 mg (98%) of an amorphous yellow product, homogeneous by TLC. (SiO_2 plates; $CHCl_3/CH_3OH$ 9:1). M.p. of the amorphous material: 141–144° (dec.). $[\alpha]_D^{23} = +147° \pm 2°$ ($c = 0.09$, $CHCl_3$). – UV. (ethanol): 213 (35160), 240 (35900), 263 (35160), 369 (8690). – IR. ($CHCl_3$): 1770 (Ar–OAc), 1735 (R–OAc). – ^{1}H-NMR. ($CDCl_3$): very similar to the spectra of hedamycin (**1**) [2] and tri-*O*-acetylkidamycin (**4**) [4], prominent signals: 2.51 (*s*, 3 H, Ar–OAc); 2.19 (*s*, 3 H, R–OAc); 2.14 (*s*, 3 H, R–OAc). – ^{13}C-NMR. ($CDCl_3$): see [3].

$C_{47}H_{56}N_2O_{14}$ (872.92) Calc. C 64.67 H 6.47 N 3.21% Found C 64.41 H 6.43 N 3.12%

Table 3. *Positional and thermal parameters assigned to hydrogen atoms*

	Atom[a])	x	y	z	U
C(21)	H(21)	0.2599 (44)	−0.1555 (47)	1.4722 (87)	0.0495 (9)
C(22)	H(22)	0.2767 (44)	−0.2549 (48)	1.2953 (86)	0.0527 (9)
C(23)	H(23)	0.3049 (44)	−0.2861 (87)	1.6820 (87)	0.0497 (9)
C(33)	H(33)	0.4632 (43)	−0.0222 (47)	0.3877 (85)	0.0489 (9)
C(34)	H(34)	0.5385 (43)	0.1279 (48)	0.2911 (85)	0.0513 (9)
C(36)	H(36)	0.6210 (44)	0.0832 (48)	0.2217 (85)	0.0493 (9)
C(39)	H(39)	0.5463 (42)	−0.0230 (46)	0.6416 (83)	0.0485 (9)
	H(39′)	0.5621 (41)	−0.0486 (47)	0.4112 (83)	0.0501 (9)

[a]) The numbering is that of *Figure 1*.

Table 4. *Bond distances and selected bond angles*[a])

Atoms[b])	Distance (Å)	Atoms[b])	Distance (Å)	Atoms[b])	Angle (°)	Atoms[b])	Angle (°)
C(1) -C(2)	1.349 (14)	C(11)-C(25)	1.556 (15)	C(1) -C(2) -C(3)	121.9 (9)	O(7) -C(28)-C(29)	105.5 (8)
C(2) -C(3)	1.463 (14)	C(25)-C(26)	1.506 (15)	C(2) -C(3) -C(4)	114.0 (9)	C(27)-C(28)-C(29)	108.9 (8)
C(3) -O(5)	1.206 (13)	C(26)-C(27)	1.554 (14)	C(3) -C(4) -C(18)	120.0 (9)	C(28)-C(29)-C(30)	112.1 (10)
C(3) -C(4)	1.507 (15)	C(27)-N(1)	1.450 (14)	C(4) -C(18)-O(1)	119.6 (9)	C(28)-C(29)-O(6)	107.8 (8)
C(4) -C(5)	1.403 (15)	N(1) -C(31)	1.494 (15)	C(18)-O(1) -C(1)	121.8 (8)	O(6) -C(29)-C(30)	103.8 (9)
C(5) -C(6)	1.495 (16)	N(1) -C(32)	1.541 (16)	O(1) -C(1) -C(2)	122.5 (9)	C(29)-O(6) -C(25)	112.1 (8)
C(5) -C(7)	1.411 (15)	C(27)-C(28)	1.513 (14)	C(2) -C(1) -C(19)	126.6 (9)	C(12)-C(13)-C(14)	117.7 (9)
C(7) -C(8)	1.399 (15)	C(28)-O(7)	1.413 (12)	O(1) -C(1) -C(19)	110.8 (8)	C(12)-C(13)-C(33)	125.0 (9)
C(8) -C(9)	1.497 (14)	C(28)-C(29)	1.575 (16)	C(1) -C(19)-C(21)	113.7 (9)	C(14)-C(13)-C(33)	117.3 (9)
C(9) -O(4)	1.246 (12)	C(29)-C(30)	1.510 (16)	C(1) -C(19)-O(8)	108.2 (8)	C(13)-C(33)-O(10)	110.6 (9)
C(9) -C(10)	1.461 (13)	C(29)-O(6)	1.454 (13)	O(8) -C(19)-C(21)	58.6 (6)	C(13)-C(33)-C(39)	113.9 (9)
C(10)-C(11)	1.400 (14)	C(25)-O(6)	1.476 (13)	C(19)-C(21)-O(8)	59.3 (7)	O(10)-C(33)-C(39)	114.4 (9)
C(11)-C(12)	1.366 (15)	C(13)-C(33)	1.527 (15)	C(19)-O(8) -C(21)	62.1 (7)	C(33)-O(10)-C(34)	117.8 (8)
C(12)-C(13)	1.365 (14)	C(33)-O(10)	1.439 (13)	C(19)-C(21)-C(22)	123.9 (10)	O(10)-C(34)-C(35)	106.6 (9)
C(13)-C(14)	1.436 (14)	C(34)-O(10)	1.442 (13)	O(8) -C(21)-C(22)	116.7 (9)	O(10)-C(34)-C(36)	112.1 (9)
C(14)-O(3)	1.340 (12)	C(34)-C(35)	1.504 (16)	C(21)-C(22)-C(23)	119.5 (10)	C(35)-C(34)-C(36)	113.6 (9)
C(14)-C(15)	1.396 (14)	C(34)-C(36)	1.507 (16)	C(21)-C(22)-O(9)	121.1 (9)	C(34)-C(36)-O(11)	110.2 (9)
C(15)-C(16)	1.486 (15)	C(36)-O(11)	1.431 (13)	C(22)-O(9) -C(23)	62.1 (8)	C(34)-C(36)-C(37)	111.0 (9)
C(16)-O(2)	1.238 (13)	C(36)-C(37)	1.551 (15)	O(9) -C(22)-C(23)	60.3 (8)	O(11)-C(36)-C(37)	112.3 (9)
C(16)-C(17)	1.530 (15)	C(37)-N(2)	1.518 (13)	C(22)-C(23)-O(9)	57.6 (7)	C(36)-C(37)-C(38)	111.1 (8)
C(17)-C(18)	1.353 (15)	N(2) -C(40)	1.472 (14)	C(22)-C(23)-C(24)	123.5 (12)	C(36)-C(37)-N(2)	106.5 (8)
C(18)-O(1)	1.386 (12)	N(2) -C(41)	1.493 (15)	O(9) -C(23)-C(24)	116.2 (11)	C(36)-C(37)-C(39)	105.4 (8)
O(1) -C(1)	1.357 (12)	C(37)-C(38)	1.548 (15)	C(10)-C(11)-C(12)	119.8 (10)	N(2) -C(37)-C(39)	105.9 (8)
C(4) -C(18)	1.412 (14)	C(37)-C(39)	1.542 (14)	C(10)-C(11)-C(25)	121.9 (9)	C(38)-C(37)-C(39)	114.6 (9)
C(8) -C(17)	1.399 (14)	C(33)-C(39)	1.543 (15)	C(12)-C(11)-C(25)	118.9 (9)	C(37)-C(39)-C(33)	116.1 (9)
C(10)-C(15)	1.399 (14)	C(21)-H(21)	1.157 (105)	C(11)-C(25)-C(26)	114.6 (9)	C(37)-N(2) -C(40)	114.8 (8)
C(1) -C(19)	1.502 (14)	C(22)-H(22)	1.142 (89)	C(11)-C(25)-O(6)	99.6 (8)	C(37)-N(2) -C(41)	112.5 (8)
C(19)-C(20)	1.506 (15)	C(23)-H(23)	1.121 (66)	O(6) -C(25)-C(26)	109.8 (9)	C(40)-N(2) -C(41)	108.7 (9)
C(19)-O(8)	1.445 (13)	C(33)-H(33)	1.133 (100)	C(25)-C(26)-C(27)	109.1 (9)		
C(19)-C(21)	1.486 (16)	C(34)-H(34)	1.009 (89)	C(26)-C(27)-N(1)	114.8 (9)		
C(21)-O(8)	1.453 (13)	C(36)-H(36)	0.852 (104)	C(26)-C(27)-C(28)	110.7 (8)		
C(21)-C(22)	1.507 (17)	C(39)-H(39)	1.245 (65)	N(1) -C(27)-C(28)	110.0 (8)		
C(22)-O(9)	1.398 (14)	C(39)-H(39')	1.080 (94)	C(27)-C(28)-O(7)	109.8 (8)		
C(22)-C(23)	1.462 (17)						
C(23)-O(9)	1.437 (15)						
C(23)-C(24)	1.501 (18)						

a) A complete list of bond angles may be obtained from one of the authors *(M.Z.)*.
b) The numbering is that of *Figure 1*.

Kidamycin (**3**) *and 11,3',3''-tri-O-acetylkidamycin* (**4**). See [3] [4]. CD. of kidamycin (1.16M in abs. ethanol, *cf. Fig. 2*): 204 (−31900), 245 (+17600), 255 (+11000), 270 (+23500), 296 (−6200), 308 (−2400), 323 (−4100), 380 (+16400).

X-ray structure determination. The systematic absences in *Weissenberg* photographs ($h00$ for $h=2n+1$, $0k0$ for $k=2n+1$ and $00l$ for $l=2n+1$) led to the space group $P2_12_12_1$. Lattice constants are $a=24.239$ (12), $b=21.440$ (10), $c=7.369$ (4) Å, $V=3829.55$ Å^3, $D_{obs.}=1.290$, $D_{calc.}=1.296$ g/cm^3 for $Z=4$. Diffractions were made on a *Philips* PW-1100, University of Ulm, FRG, using the $\theta/2\theta$ scan mode. The intensities of 2643 independent reflexions were collected in the range $2<\theta<28°$ with a fine focus molybdenum tube and a graphite monochromator to select MoK_α ($\lambda=0.71069$ Å). No absorption correction was made. The structure was solved by direct method using the program *Shelx*-76 [11]. Scattering factors for neutral atoms and terms for anomalous dispersion were taken from *Cromer et al.* [12]. Phases were calculated for those 346 $|E|$-values greater than 1.2. From the top of the convergence list 3 phases, each with one zero index for fixing the origin [13] (no ggg combination), and a restricted reflexion with no zero index for the enanthiomorph together with additional multi-solution reflexions were selected by hand. The corresponding E-*Fourier* map revealed the positions of 4 O- and 17 C-atoms. Subsequent least squares refinement and difference *Fourier* map led to the location of all atoms. All protons are localized, but only 8 were considered and refined. According to the criterion $(F_o)>1\sigma(F_o)$, 2289 reflexions were used in the anisotropic refinement steps. All parameters converged. A final difference *Fourier* map showed no electron density peak larger than 1.14 e/Å^3, the R-index is 0.091 ($R=\Sigma\|F_o|-|F_c\|/\Sigma|F_o|$). Atomic positional and thermal parameters are given in *Table 2*, positional parameters of relevant H-atoms are given in *Table 3*, while interatomic distances and selected bond angles are listed in *Table 4*.

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