HERBIMYCIN A: AN ANSAMYCIN ANTIBIOTIC; X-RAY CRYSTAL STRUCTURE

Sir:

Herbimycins are new potent herbicidal antibiotics[1] isolated from the cultured filtrate of *Streptomyces hygroscopicus* AM-3672, and also show anti-tobacco mosaic virus activity. We have proposed the ansachain structure[2] including a benzoquinone nucleus for herbimycin A based on ^{1}H- and ^{13}C-nmr spectral analyses and biosynthetic means using ^{13}C-labeled precursors. In order to determine the configuration at C-6, C-7, C-10, C-11, C-12, C-14 and C-15 in the ansachain moiety, a single crystal X-ray diffraction analysis was carried out. Herbimycin A was crystallized from benzene to afford yellowish plates, m.p. 230°C.

Crystal data are as follows: $C_{30}H_{42}N_2O_9$, M.W. 574, orthorhombic, space group $P2_12_12_1$, a=17.207 (3), b=24.608 (6), c=7.4274 (9)Å, Z=4, D_c=1.214 g cm^3. 2,857 unique intensity data for $2\theta<140°$ were collected on an automatic, four-circle diffractometer with graphite-monochromated Cu-Kα radiation using the θ-2θ scanning technique. The structure was elucidated by the Monte Carlo direct method[3] using the 40 strongest reflections as a starting set. The 164th phase set which showed a low R_k-value[4] of 28.2% led to the correct solution; an E-map based on 669 phases yielded all 41 independent non-hydrogen atoms. The structure thus obtained was refined by the block-diagonal matrix least-squares method with anisotropic temperature factors. After 30 hydrogen atoms had been located in a difference FOURIER map, several cycles of the least-squares calculations were carried out including these hydrogen atoms. The final atomic coordinates and bond distances are listed in Tables 1

Fig. 1. A perspective view of the herbimycin A molecule.

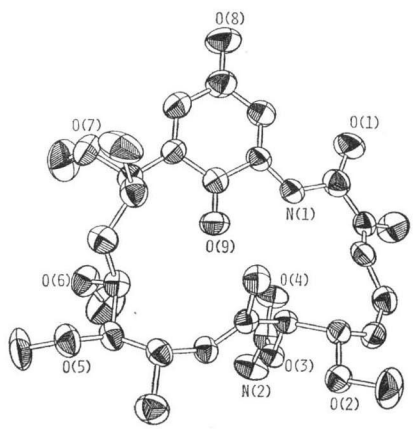

Table 1. Final atomic coordinates.

Atom	x	y	z
O(1)	0.2031 (2)	−0.0854 (1)	0.3022 (5)
O(2)	−0.1505 (1)	−0.0559 (1)	0.9257 (3)
O(3)	−0.1484 (1)	0.0009 (1)	0.5823 (3)
O(4)	−0.0655 (1)	−0.0052 (1)	0.3427 (3)
O(5)	−0.1153 (2)	0.2339 (1)	0.9094 (4)
O(6)	−0.0473 (2)	0.2180 (1)	0.5267 (4)
O(7)	0.1649 (2)	0.2263 (1)	0.4870 (5)
O(8)	0.3616 (2)	0.0785 (1)	0.3598 (5)
O(9)	0.0585 (2)	0.0753 (1)	0.4646 (5)
N(1)	0.1190 (2)	−0.0169 (1)	0.3742 (5)
N(2)	−0.1942 (2)	0.0112 (2)	0.3029 (4)
C(1)	0.1377 (2)	−0.0710 (2)	0.3444 (6)
C(2)	0.0715 (2)	−0.1083 (1)	0.3681 (6)
C(3)	0.0253 (2)	−0.0996 (1)	0.5112 (6)
C(4)	−0.0476 (2)	−0.1266 (1)	0.5549 (6)
C(5)	−0.0978 (2)	−0.1077 (2)	0.6786 (6)
C(6)	−0.0873 (2)	−0.0596 (1)	0.7986 (5)
C(7)	−0.0827 (2)	−0.0048 (1)	0.7028 (5)
C(8)	−0.0764 (2)	0.0445 (1)	0.8249 (5)
C(9)	−0.1250 (2)	0.0857 (1)	0.8167 (5)
C(10)	−0.1245 (2)	0.1374 (1)	0.9217 (5)
C(11)	−0.1132 (2)	0.1868 (2)	0.7979 (5)
C(12)	−0.0396 (2)	0.1842 (2)	0.6836 (5)
C(13)	0.0331 (2)	0.2033 (2)	0.7799 (6)
C(14)	0.1087 (2)	0.1734 (2)	0.7278 (6)
C(15)	0.1267 (2)	0.1760 (1)	0.5246 (6)
C(16)	0.1725 (2)	0.1284 (1)	0.4642 (6)
C(17)	0.2487 (2)	0.1272 (2)	0.4361 (6)
C(18)	0.2903 (2)	0.0776 (2)	0.3823 (6)
C(19)	0.2464 (2)	0.0270 (2)	0.3588 (6)
C(20)	0.1699 (2)	0.0265 (2)	0.3848 (6)
C(21)	0.1291 (2)	0.0769 (2)	0.4400 (6)
C(22)	0.0646 (3)	−0.1537 (2)	0.2363 (7)
C(23)	−0.1487 (3)	−0.1008 (2)	1.0571 (6)
C(24)	−0.1299 (2)	0.0019 (2)	0.4026 (5)
C(25)	−0.0050 (2)	0.0424 (1)	0.9458 (6)
C(26)	−0.2010 (2)	0.1426 (2)	1.0276 (6)
C(27)	−0.1397 (3)	0.2826 (2)	0.8180 (7)
C(28)	−0.0934 (3)	0.1928 (2)	0.3840 (6)
C(29)	0.1775 (3)	0.1916 (2)	0.8388 (7)
C(30)	0.1427 (3)	0.2518 (2)	0.3221 (7)

Fig. 2. Structure of herbimycin A.

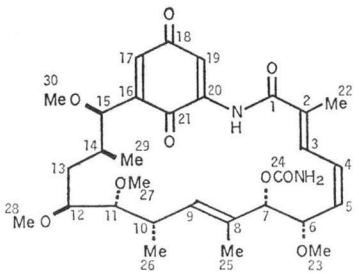

Table 2. Bond distances (1/Å).

C(1)–C(2)	1.473 (5)	C(13)–C(14)	1.544 (6)
C(1)–O(1)	1.220 (5)	C(14)–C(15)	1.543 (6)
C(1)–N(1)	1.389 (5)	C(14)–C(29)	1.512 (6)
C(2)–C(3)	1.344 (6)	C(15)–C(16)	1.481 (5)
C(2)–C(22)	1.490 (6)	C(15)–O(7)	1.429 (4)
C(3)–C(4)	1.455 (5)	C(16)–C(17)	1.327 (5)
C(4)–C(5)	1.345 (6)	C(16)–C(21)	1.482 (5)
C(5)–C(6)	1.491 (5)	C(17)–C(18)	1.472 (6)
C(6)–C(7)	1.527 (5)	C(18)–C(19)	1.466 (6)
C(6)–O(2)	1.442 (4)	C(18)–O(8)	1.238 (5)
C(7)–C(8)	1.519 (5)	C(19)–C(20)	1.329 (5)
C(7)–O(3)	1.449 (4)	C(20)–C(21)	1.482 (5)
C(8)–C(9)	1.316 (5)	C(20)–N(1)	1.383 (5)
C(8)–C(25)	1.524 (5)	C(21)–O(9)	1.230 (5)
C(9)–C(10)	1.492 (5)	C(23)–O(2)	1.475 (5)
C(10)–C(11)	1.536 (5)	C(24)–O(3)	1.372 (4)
C(10)–C(26)	1.540 (5)	C(24)–O(4)	1.208 (4)
C(11)–C(12)	1.526 (5)	C(24)–N(2)	1.350 (5)
C(11)–O(5)	1.424 (4)	C(27)–O(5)	1.440 (5)
C(12)–C(13)	1.517 (5)	C(28)–O(6)	1.464 (5)
C(12)–O(6)	1.437 (5)	C(30)–O(7)	1.429 (6)

and 2, respectively. The final R value was 6.3%.

Thus, the structure and relative configuration of herbimycin A have been established as shown in Figs. 1 and 2 except for the absolute configuration.

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References

1) ŌMURA, S.; Y. IWAI, Y. TAKAHASHI, N. SADAKANE, A. NAKAGAWA, H. ŌIWA, Y. HASEGAWA & T. IKAI: Herbimycin, a new antibiotic produced by a strain of *Streptomyces*. J. Antibiotics 32: 255~261, 1979
2) ŌMURA, S.; A. NAKAGAWA & N. SADAKANE: Structure of herbimycin, a new ansamycin antibiotic. Tetrahed. Lett. 1979: 4323~4326, 1979
3) FURUSAKI, A.: A new Monte Carlo method for phase determination. Acta Cryst. (A) 35: 220~224, 1979
4) KARLE, J. & I. L. KARLE: The symbolic addition procedure for phase determination for centrosymmetric and noncentrosymmetric crystals. Acta Cryst. 21: 849~859, 1966

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