Communications to the editor

STRUCTURE OF ENTEROCIN; X-RAY ANALYSIS OF *m*-BROMOBENZOYL ENTEROCIN DIHYDRATE

Sir:

An antibiotic enterocin was obtained from *Streptomyces candidus* var. *enterostaticus* and *S. viridochromogenes* var. M-127 which were isolated from soil samples. Enterocin has static activities against gram-positive and gram-negative bacteria[1]. Chemical and spectroscopic investigations of enterocin accounted for four hydroxyl groups, a 4-methoxy-2-oxo-pyrone and a benzoyl ring, but the structure of the skeleton remained unknown. X-Ray crystallographic analysis of *m*-bromobenzoyl enterocin dihydrate was therefore undertaken to establish the molecular structure of enterocin. The present study revealed that the major skeleton of enterocin was a unique tricyclic structure containing a γ-lactone.

m-Bromobenzoyl enterocin was obtained by treating enterocin with *m*-bromobenzoyl chloride in the presence of pyridine. Crystals suitable for X-ray work were obtained from an ethyl acetate-ethanol mixture as colorless plates. Unit-cell dimensions were determined by a least-squares calculation using the high-angle reflections of CuK_{α_1} and CuK_{α_2} on zero-layer Weissenberg photographs, on which were superimposed Al wire patterns for calibration. The density was measured by floatation in a benzene-carbon tetrachloride mixture. Crystal data are as follows: $C_{29}O_{11}H_{23}Br \cdot 2H_2O$, mp 163~167°C, MW 664.4, orthorhombic, $a = 13.61(1)$, $b = 26.61(1)$, $c = 7.73(1)$Å, $D_m = 1.55$, $D_c = 1.58 g/cm^3$, $Z = 4$. The systematic absence of the odd orders of the h00, 0k0 and 001 reflections were observed, hence the space group was found to be $P2_12_12_1$. A total of 2,306 non-zero reflections, out of a possible 2,733, was measured visually from equi-inclination Weissenberg photographs (CuK_α radiation). The structure has been refined to an R-factor of 0.14 on the observed reflections (0.17 for all 2,733 reflections) using block-diagonal least squares methods and assigning anisotropic thermal parameters to only the bromine atom. In the difference map calculated at this stage, there is no positive region exceeding 1.3 e.Å^{-3}.

The final atomic coordinates and isotropic temperature factors are given in Table 1, and the anisotropic temperature factors for the bromine atom in Table 2. The atoms O(41) and O(42) are the oxygen atoms of the water molecules of hydration. The established molecular structure of *m*-bromobenzoyl enterocin is shown in Fig. 1. A perspective drawing of *m*-bromobenzoyl enterocin is shown in Fig. 2. The enterocin derivative consists of four main fragments, *i.e.*, the tricyclic portion, the α-pyrone, the benzoyl, and the *m*-bromobenzoyl rings. Within the tricyclic portion, the six-membered ring *B* is in a chair conformation with C(5) and C(8) displaced from the plane of the four remaining atoms. The five-membered ring *A* is in a C_2 type conformation with a two-fold axis going through C(3) and the midpoint of the C(5)-C(6) bond.

Fig. 1. Structure of *m*-bromobenzoyl enterocin

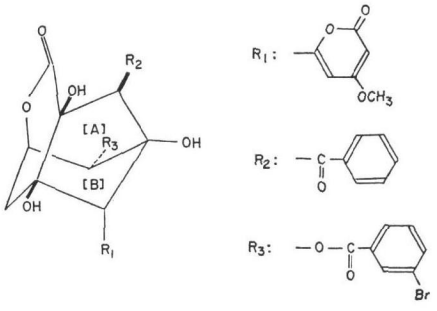

Fig. 2. Perspective drawing of *m*-bromobenzoyl enterocin.

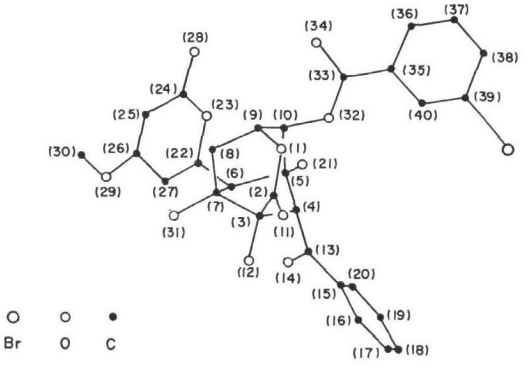

Table 1. The fractional atomic coordinates, isotropic temperature factors (Å²) and their standard deviations in parentheses.

Atom	x	y	z	B
Br	−0.0212 (2)	0.6153 (4)	0.3294 (4)	
O (1)	−0.0107 (8)	0.3665 (4)	0.5715 (16)	1.9 (2)
C (2)	0.0887 (11)	0.3584 (5)	0.5800 (24)	1.6 (2)
C (3)	0.1364 (10)	0.3422 (5)	0.4155 (22)	1.0 (2)
C (4)	0.1189 (9)	0.3858 (5)	0.2818 (21)	0.9 (2)
C (5)	0.0380 (9)	0.3640 (4)	0.1682 (21)	0.8 (2)
C (6)	0.0714 (8)	0.3091 (4)	0.1438 (20)	0.5 (2)
C (7)	0.0823 (9)	0.2936 (4)	0.3333 (21)	0.8 (2)
C (8)	−0.0178 (10)	0.2869 (5)	0.4225 (22)	1.4 (2)
C (9)	−0.0620 (10)	0.3389 (5)	0.4364 (23)	1.4 (2)
C (10)	−0.0621 (9)	0.3668 (5)	0.2620 (21)	1.1 (2)
O (11)	0.1312 (9)	0.3706 (4)	0.7090 (19)	2.7 (2)
O (12)	0.2363 (7)	0.3331 (4)	0.4389 (16)	1.5 (2)
C (13)	0.2120 (9)	0.3972 (4)	0.1876 (22)	1.0 (2)
O (14)	0.2308 (8)	0.3768 (4)	0.0428 (17)	1.8 (2)
C (15)	0.2823 (10)	0.4343 (5)	0.2615 (23)	1.4 (2)
C (16)	0.3528 (14)	0.4549 (7)	0.1366 (31)	2.9 (3)
C (17)	0.4208 (16)	0.4902 (8)	0.2157 (34)	3.9 (4)
C (18)	0.4256 (15)	0.4997 (7)	0.3732 (32)	3.4 (4)
C (19)	0.3565 (15)	0.4777 (8)	0.5011 (34)	3.6 (4)
C (20)	0.2848 (13)	0.4462 (6)	0.4239 (28)	2.4 (3)
O (21)	0.0207 (7)	0.3906 (3)	0.0081 (14)	1.0 (1)
C (22)	0.0156 (9)	0.2742 (4)	0.0321 (20)	0.7 (2)
O (23)	−0.0823 (7)	0.2835 (3)	0.0106 (15)	1.0 (1)
C (24)	−0.1383 (11)	0.2553 (5)	−0.1018 (23)	1.6 (3)
C (25)	−0.0941 (11)	0.2141 (5)	−0.1973 (25)	1.6 (2)
C (26)	0.0027 (10)	0.2056 (5)	−0.1644 (24)	1.5 (2)
C (27)	0.0612 (10)	0.2368 (5)	−0.0567 (23)	1.4 (2)
O (28)	−0.2251 (9)	0.2690 (4)	−0.1144 (19)	2.6 (2)
O (29)	0.0565 (8)	0.1710 (4)	−0.2488 (18)	2.3 (2)
C (30)	0.0024 (15)	0.1400 (7)	−0.3740 (31)	3.5 (4)
O (31)	0.1358 (7)	0.2491 (3)	0.3574 (16)	1.4 (2)
O (32)	−0.0827 (7)	0.4196 (3)	0.2917 (15)	1.1 (2)
C (33)	−0.1773 (11)	0.4326 (5)	0.2982 (26)	1.8 (3)
O (34)	−0.2440 (9)	0.4027 (4)	0.2913 (20)	2.8 (2)
C (35)	−0.1943 (11)	0.4871 (5)	0.3026 (26)	1.9 (3)
C (36)	−0.2893 (14)	0.5064 (7)	0.3147 (33)	3.4 (4)
C (37)	−0.3046 (19)	0.5583 (9)	0.3227 (43)	5.2 (5)
C (38)	−0.2305 (18)	0.5886 (9)	0.3250 (40)	4.8 (5)
C (39)	−0.1304 (16)	0.5700 (8)	0.3250 (36)	4.0 (4)
C (40)	−0.1129 (11)	0.5197 (6)	0.3063 (27)	2.0 (3)
O (41)	0.3159 (11)	0.3115 (5)	0.7603 (23)	3.9 (3)
O (42)	0.2421 (10)	0.2180 (5)	0.6573 (23)	3.7 (3)

Table 2. Anisotropic temperature factors for bromine atom (their standard deviations).

The anisotropic temperature factors are expressed in the form of $\exp[-(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+\beta_{12}hk+\beta_{13}hl+\beta_{23}kl)]$

Atom	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Br	0.0094 (0.0002)	0.0010 (0.0001)	0.0210 (0.0006)	−0.0005 (0.0001)	−0.0014 (0.0003)	−0.0003 (0.0001)

YOJI TOKUMA
NORIMASA MIYAIRI
YUKIYOSHI MORIMOTO
Research Laboratories,
Fujisawa Pharmaceutical Co., Ltd.,
Yodogawa-ku, Osaka 532, Japan
(Received October 29, 1975)

Reference

1) MIYAIRI, N.; H. SAKAI, T. KONOMI & H. IMANAKA: Enterocin, a new antibiotic. J. Antibiotics 29: 227~235, 1976