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# Crystal and Molecular Structure of 9-deoxo-9a-ethyl-9a-aza-9a-homoerythronolide A*

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The title compound is the 15-membered aglycone ring of the *N*-ethyl derivative of the new semisynthetic macrolide antibiotic 9-deoxo-9a-aza-9a-homoerythromycin A. Its molecular and crystal structure has been determined from the diffractometer X-ray intesity data and refined by the least-squares method to the reliability index R = 0.064. The crystals are orthorhombic, space group $P2_12_12_1$, with cell parameters $a$ = 17.784 (5), $b$ = 22.009 (5), $c$ = 13.675 (3) Å. Although the molecular structure is similar to the analogous *N*-methyl derivative, as well as to other compounds with such 15-membered aglycone rings, the packing of molecules in the crystal structure is significantly different. In the present structure, all hydroxyl-hydrogen atoms of the aglycones take part in the hydrogen bondings between neighbouring molecules forming helices around each screw diad axis. The helices are interconnected by an additional hydrogen bond.

* The analogous N-methyl derivative was published under the equivalent name 10,10-dihydro-10-deoxo-10a--methyl-10a-aza-10a-homoerythronolide A[10].

## INTRODUCTION

This structural investigation is a part of our broader research on 9-deoxo-9a-aza-9a-homoerythromycin A derivatives, the new semisynthetic macrolide antibiotics with the 15-membered aglycone rings.[1,2] 9-deoxo-9a-methyl-9a-aza-9a-homoerythromycin A (Azithromycin) differs structurally from erythromycin due to the insertion of an additional 9a-methyl-substituted nitrogen in the 14-membered aglycone ring. Compared to erythromycin, this modification shows a significant improvement in potency against Gram-negative bacteria and superior pharmacokinetic properties producing high and sustained tissue concentrations. [3, 4] Azithromycin has recently been launched in Yugoslavia under the trade name SUMAMED and jointly with Pfizer Inc. it is subjected to further clinical trials.

The title compound, *i. e.* the corresponding 9a-ethyl analogue, was obtained by a straightforward reductive alkylation of 9-deoxo-9a-aza-9a-homoerythromycin A with acetaldehyde. [5] The acidcatalyzed degradation of this compound caused cleavage of both sugars, L-cladinose and D-desosamine, and yielded 9-deoxo-9a-ethyl-9a-aza-9a-homoerythronolide A. [6] The same compound was prepared also by reductive alkylation of 9-deoxo-9a-aza-9a-homoerythronolide A.

## EXPERIMENTAL

### *Crystal Data*

From oscillation and Weissenberg photographs and single crystal diffractometry, CuK$\alpha$, $\lambda = 1.5418$ Å, $C_{23}H_{45}NO_7$, $a$ = 17.784 (5), $b$ = 22.009 (5), $c$ = 13.675 (3) Å, $V$ = 5352 (2) Å$^3$, $Z$ = 4 (two independent molecules in the asymmetric unit), $D_{obs}$ = 1.112 (6) Mg.m$^{-3}$ (by flotation), $D_{calc}$ = 1.111 Mg.m$^{-3}$, $F$ (000) = 1968, $\mu$ (CuK$\mu$) = 5.83 cm$^{-1}$, orthorhombic, space group $P\ 2_12_12_1$.

### *Intensity Data, Structure Determination and Refinement*

The lattice parameters were obtained by least-squares refinement of 16 reflections within $16.4 \leq \theta \leq 22$ °. The integrated intesities of 4539 independent reflections from a specimen of dimensions 0.38 x 0.39 x 0.50 mm$^3$ within the interval $3 \leq \theta \leq 70$ ° were collected on an automatic diffractometer Philips PW1100 (graphite monochromatized CuK$\alpha$ radiation, $\theta$–$2\theta$ scan technique, scan range 1.2 °, scan rate 0.04 °s$^{-1}$). Intesities of three standard reflections, monitored every two hours, showed no significant crystal decomposition (8.8%). The 4455 reflections with $I > 3\sigma(I)$ were used in the structure analysis and refinement. The data were corrected for Lorentz and polarization factors but not for absorbtion.

About half of all non-hydrogen atoms were obtained by using the SIR programme, [7] the remaining atoms from the successive Fourier syntheses and then refined anisotropically using SHELX 76.[8] Hydrogen atoms were located either in a difference Fourier map or generated from the assumed geometries, except for hydrogens H (0141) and H(041) of molecule (A) and H(041), H(061) and H(0131) of molecule (B). They were then, as riding atoms,included in the structure factor calculations. The final value of the reliability index was $R$ = 0.064. Unit weights were assumed for all observations. Maximum and minimum peak heights in the final difference Fourier map were +0.27 and –0.27 eA$^{-3}$, respectively. The atomic scattering factors were from the International Table for X-ray Crystallography.[9]

Final values of atomic coordinates are given in Table I. A list of observed and calculated structure factors can be obtained from the authors on request. All calculations were perfomed on an IBM PC/AT compatibile microcomputer (procesor 80336/20MHz and mathematical coprocessor 80387).

TABLE I

*Atomic coordinates ($x10^4$) and equivalent isotropic thermal parameters * ($x10^3 Å^2$) for non-H atoms for both crystallographically independent molecules (A) and(B)*

| | Molecule (A) | | | | Molecule (B) | | | |
|---|---|---|---|---|---|---|---|---|
| | X | Y | Z | $U_{eq}$ | X | Y | Z | $U_{eq}$ |
| O(1) | 5518(3) | 4254(2) | 6480(4) | 59(1) | 3446(2) | 7414(2) | 3938(3) | 48(1) |
| C(2) | 4793(4) | 4293(3) | 6342(5) | 55(2) | 3395(4) | 6807(3) | 3848(5) | 47(2) |
| O(21) | 4464(3) | 4735(3) | 6079(5) | 83(2) | 2839(3) | 6542(2) | 3612(5) | 74(2) |
| C(3) | 4385(5) | 3701(3) | 6573(5) | 61(2) | 4131(4) | 6499(3) | 4074(5) | 46(1) |
| C(31) | 3930(6) | 3508(5) | 5689(7) | 109(3) | 4344(5) | 6103(4) | 3197(6) | 72(2) |
| C(4) | 3886(4) | 3799(3) | 7478(5) | 51(2) | 4040(3) | 6122(3) | 5001(5) | 45(2) |
| O(41) | 3471(3) | 3255(2) | 7630(4) | 70(1) | 4741(3) | 5811(2) | 5151(4) | 67(1) |
| C(5) | 4340(3) | 3967(3) | 8407(5) | 44(1) | 3825(3) | 6503(3) | 5908(5) | 41(1) |
| C(51) | 4874(4) | 3446(3) | 8727(6) | 58(2) | 4464(4) | 6945(3) | 6202(6) | 62(2) |
| C(6) | 3801(4) | 4197(3) | 9230(5) | 47(2) | 3549(3) | 6080(3) | 6747(5) | 43(1) |
| O(61) | 3638(3) | 3693(2) | 9872(3) | 54(1) | 4160(2) | 5970(2) | 7414(3) | 54(1) |
| C(7) | 4086(4) | 4755(3) | 9815(5) | 47(2) | 2842(4) | 6311(3) | 7287(5) | 47(2) |
| O(71) | 4227(2) | 5226(2) | 9095(3) | 47(1) | 2272(2) | 6403(2) | 6560(3) | 46(1) |
| C(72) | 3439(4) | 4973(3) | 10484(6) | 61(2) | 2566(4) | 5808(3) | 7983(6) | 61(2) |
| C(8) | 4818(4) | 4619(3) | 10376(5) | 54(2) | 3001(4) | 6919(3) | 7833(5) | 52(2) |
| C(9) | 5135(5) | 5141(3) | 11004(5) | 63(2) | 2337(4) | 7186(4) | 8428(5) | 62(2) |
| C(91) | 5447(6) | 4891(4) | 11980(6) | 84(3) | 2617(6) | 7446(5) | 9405(6) | 91(3) |
| C(10) | 5780(5) | 5482(4) | 10523(6) | 79(2) | 1933(5) | 7701(4) | 7912(6) | 67(2) |
| N(11) | 5615(4) | 5682(3) | 9500(5) | 66(2) | 1680(3) | 7559(3) | 6890(4) | 53(1) |
| C(111) | 5469(6) | 6363(4) | 9458(7) | 90(3) | 844(4) | 7461(4) | 6853(7) | 72(2) |
| C(112) | 4792(6) | 6584(4) | 9968(8) | 102(3) | 580(5) | 6899(4) | 7397(8) | 90(3) |
| C(12) | 6229(4) | 5460(4) | 8843(6) | 67(2) | 1952(4) | 8036(3) | 6196(5) | 53(2) |
| C(121) | 6940(5) | 5856(5) | 8865(8) | 102(3) | 1448(4) | 8608(3) | 6189(7) | 70(2) |
| C(13) | 5934(4) | 5337(3) | 7790(5) | 56(2) | 2101(4) | 7752(3) | 5170(5) | 46(2) |
| O(131) | 5770(2) | 5888(2) | 7277(4) | 58(1) | 1411(3) | 7579(2) | 4708(4) | 56(1) |
| C(14) | 6462(4) | 4954(3) | 7121(6) | 61(2) | 2520(4) | 8180(3) | 4441(5) | 48(2) |
| O(141) | 7094(2) | 5307(2) | 6819(4) | 75(2) | 1973(3) | 8589(2) | 4042(4) | 67(1) |
| C(142) | 6803(4) | 4394(4) | 7638(7) | 79(2) | 3150(4) | 8560(3) | 4897(6) | 61(2) |
| C(15) | 6071(4) | 4767(3) | 6207(6) | 61(2) | 2821(4) | 7798(3) | 3585(5) | 52(2) |
| C(151) | 6490(5) | 4553(4) | 5344(7) | 84(3) | 3153(5) | 8169(4) | 2739(6) | 75(2) |
| C(152) | 6016(6) | 4423(5) | 4446(7) | 109(4) | 3325(7) | 7777(5) | 1849(6) | 111(4) |

* $U_{eq}$ is defined as one third of the trace of the orthogonalized $U_{ij}$ tensor

## *Description of the Structure and Discussion*

Selected interatomic distances and angles, together with their standard deviations, are given in Table II, the perspective view of the molecular structure in Figure 1. A general feature of the aglycone molecules are their 15-membered rings with bond lenghts and angles identical or very similar to those already found in the structures of the analogous aglycones as well as in 9-deoxo-9a-methyl-9a-aza-9a-homoerythromycin A itself. [1, 2, 10] In comparison with the crystal structure of *N*-methyl derivative, with one crystallographically independent molecule per unit cell, the crystal structure of the *N*-ethyl derivative contains two crystalographically independent molecules (A) and (B) but with essentially the same conformation. Table III gives the torsion angles in the molecules (A) and (B) of the *N*-ethyl derivative compared to such angles in the *N*-methyl derivative as well as in both azithromycin and erythromycin. [2, 11] As it can be seen, the conformational angles follow the same general pattern as those in the analogous 14-membered ring structure, except of course, in the regions of the alkylated nitrogen atoms. Further, the removal of both sugar components did not change the conformation of the aglycone rings.

TABLE II

*Interatomic distances (Å) and angles (°) for both crystallographically independent molecules (A) and (B)*

**(a) Bond lengths**

| | | (A) | (B) |
|---|---|---|---|
| O(1) | – C(2) | 1.306 (9) | 1.345 (8) |
| O(1) | – C(15) | 1.484 (8) | 1.477 (8) |
| C(2) | – O(21) | 1.191 (9) | 1.193 (9) |
| C(2) | – C(3) | 1.524(10) | 1.506(10) |
| C(3) | – C(31) | 1.516(13) | 1.531(11) |
| C(3) | – C(4) | 1.538(10) | 1.524(10) |
| C(4) | – O(41) | 1.422 (8) | 1.437 (8) |
| C(4) | – C(5) | 1.550 (9) | 1.545 (9) |
| C(5) | – C(51) | 1.552 (9) | 1.549 (9) |
| C(5) | – C(6) | 1.563 (9) | 1.557 (9) |
| C(6) | – O(61) | 1.444 (8) | 1.439 (7) |
| C(6) | – C(7) | 1.551(10) | 1.544 (9) |
| C(7) | – O(71) | 1.451 (8) | 1.434 (8) |
| C(7) | – C(72) | 1.546(10) | 1.540(10) |
| C(7) | – C(8) | 1.540(10) | 1.558 (9) |
| C(8) | – C(9) | 1.541(10) | 1.550(10) |
| C(9) | – C(91) | 1.547(11) | 1.536(11) |
| C(9) | – C(10) | 1.520(12) | 1.516(12) |
| C(10) | – N(11) | 1.496(11) | 1.501(10) |
| N(11) | – C(111) | 1.522(11) | 1.503 (9) |
| N(11) | – C(12) | 1.496(10) | 1.496 (9) |
| C(111) | – C(112) | 1.474(15) | 1.518(13) |
| C(12) | – C(121) | 1.536(12) | 1.545(10) |
| C(12) | – C(13) | 1.556(11) | 1.559(10) |
| C(13) | – O(131) | 1.431 (8) | 1.432 (9) |
| C(13) | – C(14) | 1.559(10) | 1.561(10) |
| C(14) | – O(141) | 1.427 (8) | 1.433 (9) |
| C(14) | – C(142) | 1.545(11) | 1.531(10) |
| C(14) | – C(15) | 1.536(11) | 1.537(10) |
| C(15) | – C(151) | 1.524(12) | 1.534(11) |
| C(151) | – C(152) | 1.517(14) | 1.532(13) |

**(b) Bond angles**

| | | | (A) | (B) |
|---|---|---|---|---|
| C(2) | – O(1) | – C(15) | 120.3(6) | 119.2(5) |
| O(1) | – C(2) | – O(21) | 125.6(7) | 124.5(6) |
| O(1) | – C(2) | – C(3) | 112.6(6) | 111.7(6) |
| O(21) | – C(2) | – C(3) | 121.8(7) | 123.8(6) |
| C(2) | – C(3) | – C(31) | 109.2(7) | 108.1(6) |
| C(2) | – C(3) | – C(4) | 108.8(6) | 108.9(6) |
| C(31) | – C(3) | – C(4) | 111.9(7) | 111.5(6) |
| C(3) | – C(4) | – O(41) | 107.4(6) | 106.6(5) |
| C(3) | – C(4) | – C(5) | 113.1(6) | 113.5(5) |
| O(41) | – C(4) | – C(5) | 110.6(5) | 111.0(5) |
| C(4) | – C(5) | – C(51) | 111.9(5) | 111.6(5) |
| C(4) | – C(5) | – C(6) | 110.4(5) | 110.2(5) |
| C(51) | – C(5) | – C(6) | 114.3(5) | 114.6(5) |
| C(5) | – C(6) | – O(61) | 108.2(5) | 109.2(5) |
| C(5) | – C(6) | – C(7) | 115.3(5) | 114.3(5) |
| O(61) | – C(6) | – C(7) | 111.1(5) | 111.5(5) |

TABLE II – cont.'d

**(b) Bond angles**

| | | | (A) | (B) |
|---|---|---|---|---|
| C(6) | – C(7) | – O(71) | 105.8(5) | 106.9(5) |
| C(6) | – C(7) | – C(72) | 107.9(6) | 108.6(5) |
| C(6) | – C(7) | – C(8) | 112.3(6) | 111.4(5) |
| O(71) | – C(7) | – C(72) | 108.0(5) | 107.7(5) |
| O(71) | – C(7) | – C(8) | 109.3(5) | 109.8(5) |
| C(72) | – C(7) | – C(8) | 113.2(6) | 112.3(6) |
| C(7) | – C(8) | – C(9) | 116.2(6) | 116.0(6) |
| C(8) | – C(9) | – C(91) | 110.3(6) | 110.5(7) |
| C(8) | – C(9) | – C(10) | 113.8(6) | 113.6(6) |
| C(91) | – C(9) | – C(10) | 106.2(7) | 106.3(7) |
| C(9) | – C(10) | – N(11) | 113.7(7) | 114.8(7) |
| C(10) | – N(11) | – C(111) | 111.0(7) | 111.0(6) |
| C(10) | – N(11) | – C(12) | 108.8(6) | 110.3(6) |
| C(111) | – N(11) | – C(12) | 115.1(7) | 113.5(6) |
| N(11) | – C(111) | – C(112) | 116.5(8) | 114.0(7) |
| N(11) | – C(12) | – C(121) | 113.8(7) | 112.8(6) |
| N(11) | – C(12) | – C(13) | 111.5(6) | 110.2(5) |
| C(121) | – C(12) | – C(13) | 113.2(7) | 114.8(6) |
| C(12) | – C(13) | – O(131) | 112.0(6) | 111.0(5) |
| C(12) | – C(13) | – C(14) | 115.7(6) | 114.5(6) |
| O(131) | – C(13) | – C(14) | 107.1(5) | 106.7(5) |
| C(13) | – C(14) | – O(141) | 110.5(6) | 107.3(5) |
| C(13) | – C(14) | – C(142) | 113.5(6) | 114.8(6) |
| C(13) | – C(14) | – C(15) | 108.2(6) | 108.8(5) |
| O(141) | – C(14) | – C(142) | 104.9(6) | 108.0(5) |
| O(141) | – C(14) | – C(15) | 108.4(6) | 106.9(5) |
| C(142) | – C(14) | – C(15) | 111.2(6) | 110.7(6) |
| O(1) | – C(15) | – C(14) | 107.9(6) | 109.0(5) |
| O(1) | – C(15) | – C(151) | 106.8(6) | 105.2(5) |
| C(14) | – C(15) | – C(151) | 115.4(6) | 114.7(6) |
| C(15) | – C(151) | – C(152) | 112.2(7) | 112.2(7) |

**(c) Inter and intramolecular hydrogen bonds**

| | | | |
|---|---|---|---|
| $O_A$ (71)...$N_A$(11) | 2.722(8) Å | $O_A$ (41)...$O_B$ ($21^i$) | 2.726(8) Å |
| $O_B$ (71)...$N_B$(11) | 2.800(8) Å | $O_A$ (61)...$O_B$($131^i$) | 2.810(6) Å |
| $O_A$ (21)...$O_B$(41) | 2.732(8) Å | $O_A$ (61)...$O_B$ ($71^i$) | 2.827(6) Å |
| $O_A$ (71)...$O_B$(61) | 2.825(6) Å | $O_A$(141)...$O_B$($141^{ii}$) | 2.709(7) Å |
| $O_A$(131)...$O_B$(61) | 2.875(5) Å | | |

Symmetry code: (i) = 0.5–x, 1–y, 0.5+z
(ii) = 0.5+x, 1.5–y, 1–z

There is, however, a significant difference in the molecular packing in the crystal structure of *N*-methyl as compared to the *N*-ethyl derivative. As shown in Figure 2, in the crystal structure of the *N*-methyl derivative only two hydroxyl-hydrogen atoms (those attached to O (61) and O (131)) participate in the intermolecular hydrogen bonding whereas in the structure of the *N*-ethyl derivative all hydroxyl-hydrogens take part in the hydrogen bonding between molecules (A) and (B) (Table II). For example, while each molecule (A) is hydrogen bonded to the neighbouring molecule (B), as well as to its symmetrically related pair ($B^i$) (i = 0.5 – x, 1 – y, 0.5 + *z*), each molecule (B) is hydrogen bonded to molecule (A) and its pair ($A^{iii}$, (iii = 0.5 – x, 1 – y, *z* – 0.5). In this way, around each 2-fold screw axis, the aglycone molecules form helices that are mutually linked

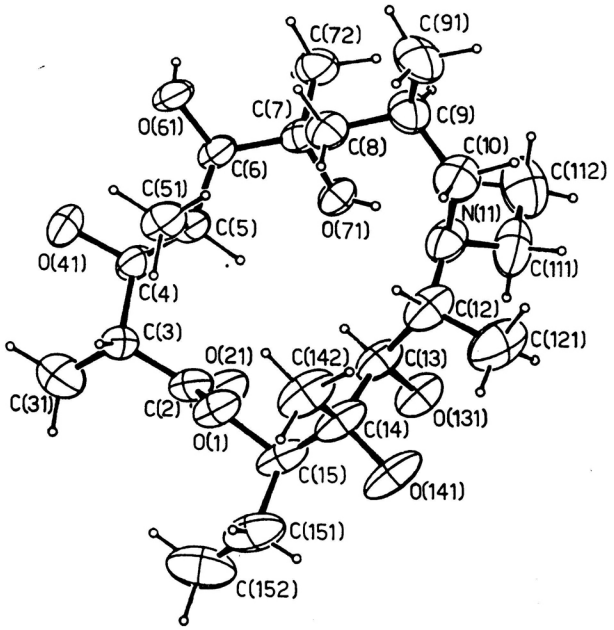
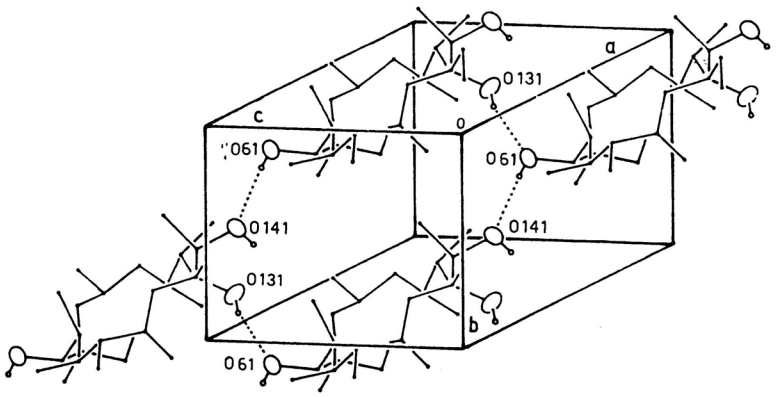



Figure 1. A perspective view of the title molecule with atom-numbering. Although there are two crystallographically independent molecules in the unit cell, both having the same conformation, only that of (A) is shown. Molecule (B) has an analogous atom-numbering scheme. Ellipsoids are drawn at the 50% level and hydrogen atoms represented by spheres of arbitrary size.

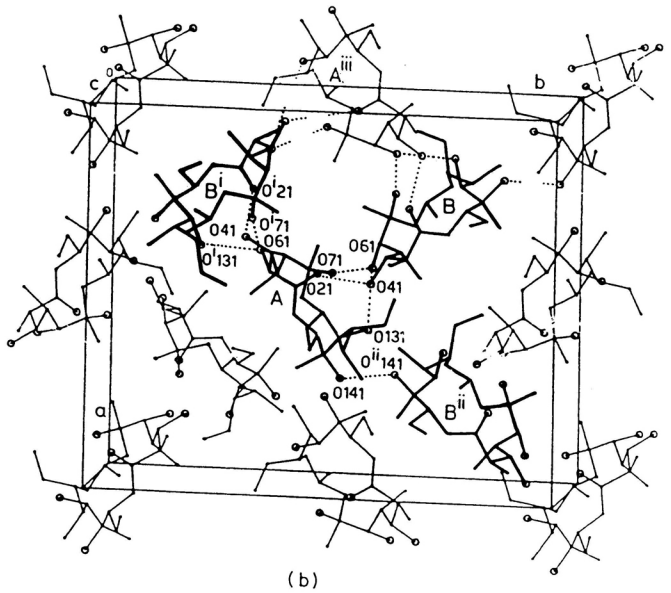
TABLE III

*A comparison of the torsion angles within the aglycone rings of the crystallographically independent molecules (A) and (B) of the title composed with those of the analogous N-methyl derivative (a),[10] azithromycin (b)[2] and erythromycin (c)[11]*

| **Torsion angles (°)** | | | | | |
|---|---|---|---|---|---|
| | (A) | (B) | (a) | (b) | (c) |
| C(15)–O(1) –C(2) –C(3) | 174.5(5) | 169.6(5) | 173.2(3) | 176.7(5) | 172.0(5) |
| O(1) –C(2) –C(3) –C(4) | 112.8(6) | 113.7(6) | 114.4(4) | 122.5(5) | 107.5(6) |
| C(2) –C(3) –C(4) –C(5) | – 62.4(7) | – 61.4(7) | – 58.9(5) | – 91.5(5) | – 84.1(6) |
| C(3) –C(4) –C(5) –C(6) | 167.6(5) | 165.9(5) | 173.1(4) | 178.8(4) | 167.2(5) |
| C(4) –C(5) –C(6) –C(7) | –138.4(6) | –136.5(5) | –146.6(4) | –109.6(5) | – 95.7(6) |
| C(5) –C(6) –C(7) –C(8) | – 62.2(7) | – 63.8(7) | – 59.8(5) | – 70.4(6) | – 73.0(6) |
| C(6) –C(7) –C(8) –C(9) | –178.2(6) | –178.4(5) | 168.2(4) | 174.9(5) | 174.8(5) |
| C(7) –C(8) –C(9) –C(10) | –100.4(7) | –101.4(7) | –107.5(4) | –109.3(6) | – 77.2(7) |
| C(8) –C(9) –C(10)–N(11) | 50.2(9) | 52.4(8) | 59.1(5) | 67.9(7) | – |
| C(9) –C(10)–N(11)–C(12) | –126.7(7) | –127.5(6) | –141.4(4) | 148.8(5) | – |
| C(10)–N(11)–C(12)–C(13) | 149.7(6) | 148.6(5) | 157.4(3) | 158.5(4) | – |
| N(11)–C(12)–C(13)–C(14) | –164.9(6) | –169.6(5) | –163.0(3) | –157.1(5) | – |
| C(12)–C(13)–C(14)–C(15) | 168.5(6) | 164.7(5) | 161.6(3) | 163.1(5) | 165.0(5) |
| C(13)–C(14)–C(15)–O(1) | – 78.0(7) | – 70.7(6) | – 75.4(4) | – 77.4(6) | – 71.5(6) |
| C(14)–C(15)–O(1) –C(2) | 123.5(6) | 121.6(6) | 123.7(3) | 121.3(5) | 125.4(6) |




(a)




(b)

Figure 2. Packing diagrams with intermolecular hydrogen bonds shown by dotted lines for *N*-methyl (a) and *N*-ethyl derivative (b). The aglycone molecules (such as $A^{iii}$, B, A and $B^{i}$) in (b) are linked together by hydrogen bonds forming helices about the screw diad axes. The helices are interconnected through the hydrogen bond $O_A$ (141)... $O_b$ ($141^{ii}$). Hydrogen bond lengths and the corresponding symmetry codes are given in Table II.

through an additional hydrogen bond $0_A$ (141)... $0_B$ ($141^{ii}$) of 2.709Å (ii = 0.5 + x, 1.5 – y, 1 – z). It is reasonable to suppose that such packing netvork is responsible for the less dense structure of the *N*-ethyl derivative. Similary as it was found in the crystal structure of *N*-methyl derivative,[10] the distances $0_A$ (71)... $N_A$ (11) and $0_B$ (71)... $N_B$ (11) of 2.722 and 2.800Å, respectively, are indicative of an intramolecular bond within each molecule.

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## REFERENCES

1. S. Djokić, G. Kobrehel, G. Lazarevski, N. Lopotar, Z. Tamburašev, B. Kamenar, A. Nagl, and I. Vicković, *J. Chem. Soc. Perkin Trans.* (1986), 1881.
2. S. Djokić, G. Kobrehel, N. Lopotar, B. Kamenar, A. Nagl, and D. Mrvoš, *J. Chem. Res. (S)*, (1988) 152; J. Chem. Res. (M) 1239.
3. J. Retsema, A. Girard, W. Schelkly, M. Manousos, M. Anderson, G. Bright, R. Borovoy, L. Brennan, and R. Mason, *Antimicrob. Agents Chemother.*,**31** (1987) 1939.
4. A. E. Girard, D. Girard, A. R. English, T. D. Gootz, C. R. Cimochowski, and J. A. Faiella, *Antimicrob. Agents Chemother.* **31** (1987) 1948.
5. G. M. Bright, A. A. Nagel, J. Bordner, K. A. Desai, J. N. Dibrino, J. Nowakowska, L. Vincent, R. M. Watrous, F. Sciavolino, A. R. English, J. A. Retsema, M. R. Anderson, L. A. Brennan, R. J. Borovoy, C. R. Cimochowski, J. A. Faiella, R. E. Girard, D. Girard, C. Herbert, M. Manousos, and R. Mason, *Journal of Antibiotics* **41** (1988) 1029.
6. S. Djokić, N. Lopotar, G. Kobrehel, H. Krnjević, and O. Carević, *US Pat.* **4** (1989) 886,792.
7. M. C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, G. Polidori, R. Spagna, and D. Viterbo, *SIR, J. Appl. Cryst.* **22** (1989) 389.
8. G. M. Sheldrick, SHELX76, *Program for Crystal Structure Determination* Univ. of Cambridge, England.
9. *International Tables for X-ray Crystallography* Vol. **IV**, Birmingham,. Kynoch Press, 1974, p. 72.
10. B. Kamenar, D. Mrvoš-Sermak, I. Vicković, and A. Nagl, *Acta Cryst.* **C46** (1990) 1964.
11. J. D. Oliver and L. C. Strickland, *Acta Cryst.* **C42** (1986) 952.

## SAŽETAK

### Kristalna i molekulska struktura 9-deoxo-9a-etil-9a-aza-9a-homoertronolida A

*Boris Kamenar, Draginja Mrvoš-Sermek, Zrinka Banić, Ante Nagl i Gabrijela Kobrehel*

Spoj u naslovu je 15-eročlani aglikonski prsten *N*-etilnog derivata novoga makrolidnog antibiotika 9-deokso-9a-aza-9a-homoeritromicina A. Molekulska i kristalna struktura određena je iz difraktometrijskih rentgenskih podataka i utočnjena metodom najmanjih kvadrata do faktora $R = 0.064$. Kristali su rompski, prostorne grupe $P2_12_12_1$, i imaju dimenzije jedinične ćelije $a = 17.784(5)$, $b = 22.009(5)$, $c = 13.675(3)$ A. Premda je ova molekulska strukturaa slična onoj u *N*-metilnom derivatu kao i u drugim spojevima s takvim 15-eročlanim aglikonskim prstenom, pakovanje molekula je značajno drugačije. U ovoj strukturi svi vodikovi atomi hidroksilnih skupina aglikona sudjeluju u vodikovim vezama tako da se oko svake helikodalne osi drugog reda stvaraju uzvojnice. One su također međusobno povezane jednom dodatnom vodikovom vezom.