*Acta Cryst.* (1977). B**33**, 2314–2316

# 5,9-Diacetyl (3,6)Bicycloleuconolide $A_3$

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(*Received* 24 *January* 1977; *accepted* 21 *February* 1977)

**Abstract.** $C_{24}H_{34}O_8$, monoclinic, $P2_1$, $a = 11{\cdot}206$ (6), $b = 8{\cdot}248$ (4), $c = 14{\cdot}272$ (7) Å, $\beta = 107{\cdot}66$ (2)°, $Z = 2$. The structure was solved by direct methods and refined to $R = 5{\cdot}1\%$. The title compound is a 16-membered-ring lactone, with a five-membered ring branched on C(3) and C(6). The principal configurations are 3(*R*), 6(*R*) and 9(*R*).

**Introduction.** Cell parameters were determined by a least-squares refinement of axial reflexions measured by a Philips PW 1100 automatic diffractometer. Intensities were collected with graphite-monochromated Cu $K\alpha$ radiation. Measurements were carried out in the $\omega/2\theta$ mode ($\theta \leq 68°$), at a scan speed of 0·04° $s^{-1}$, with scans of 2·2 °. Background measurements of 15 s were made on both sides of each scan. 2468 intensities were retained $[I \geq 2\sigma(I)]$.

The structure was solved by the application of *MULTAN* (Germain, Main & Woolfson, 1971). At the end of the isotropic refinement ($R$ = 14%), H atoms were located from difference series. After introduction of anisotropic temperature factors for the heavy atoms, and isotropic temperature coefficients (equal to those of the bonded atom) for H, refinement of the different

Table 1. *Fractional coordinates* ($\times 10^4$) *for the heavy atoms, with e.s.d.'s in parentheses*

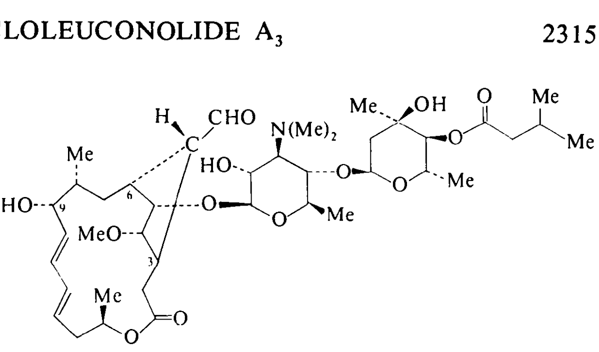
| | *x* | *y* | *z* |
|---|---|---|---|
| C(1) | 2599 (3) | 5708 (5) | 6438 (3) |
| C(2) | 3196 (3) | 5335 (5) | 7507 (2) |
| C(3) | 4256 (3) | 6475 (4) | 8023 (2) |
| C(4) | 4849 (3) | 6084 (4) | 9116 (2) |
| C(5) | 6225 (3) | 6340 (4) | 9300 (2) |
| C(6) | 6454 (3) | 5630 (4) | 8372 (2) |
| C(7) | 7778 (3) | 5825 (4) | 8321 (2) |
| C(8) | 8113 (3) | 5105 (4) | 7448 (2) |
| C(9) | 7868 (3) | 3276 (4) | 7287 (2) |
| C(10) | 6538 (3) | 2777 (4) | 6853 (2) |
| C(11) | 5744 (3) | 3335 (4) | 6019 (2) |
| C(12) | 4430 (3) | 2864 (4) | 5639 (2) |
| C(13) | 3568 (3) | 3628 (5) | 4934 (2) |
| C(14) | 2220 (3) | 3247 (5) | 4613 (2) |
| C(15) | 1402 (3) | 4464 (5) | 4924 (2) |
| C(16) | 1837 (2) | 4512 (3) | 5995 (2) |
| C(17) | 5349 (3) | 6429 (4) | 7567 (2) |
| C(18) | 5660 (4) | 8103 (6) | 7309 (3) |
| O(19) | 5581 (7) | 9285 (5) | 7613 (4) |
| O(20) | 6931 (2) | 5515 (3) | 10181 (2) |
| C(21) | 7611 (4) | 6424 (6) | 10936 (3) |
| O(22) | 7875 (3) | 7799 (5) | 10849 (2) |
| C(23) | 8035 (5) | 5465 (9) | 11855 (3) |
| O(24) | 4377 (2) | 7097 (3) | 9721 (2) |
| C(25)*A* | 3393 (9) | 6585 (11) | 10022 (6) |
| C(25)*B* | 4197 (8) | 6364 (11) | 10536 (6) |
| C(26) | 9480 (3) | 5482 (6) | 7560 (3) |
| O(27) | 8372 (2) | 2528 (3) | 8253 (1) |
| C(28) | 8757 (3) | 995 (5) | 8279 (3) |
| O(29) | 8727 (3) | 216 (4) | 7567 (3) |
| C(30) | 9235 (4) | 390 (6) | 9312 (3) |
| C(31) | 49 (4) | 4031 (7) | 4613 (3) |
| O(32) | 2796 (2) | 6910 (3) | 6030 (2) |

Table 2. *Fractional coordinates* ($\times 10^3$) *for* H *atoms, with e.s.d.'s in parentheses*

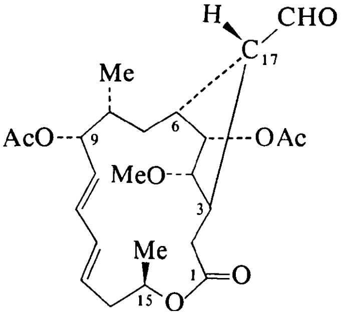
| | *x* | *y* | *z* |
|---|---|---|---|
| H(2)*A* | 268 | 503 | 781 |
| H(2)*B* | 339 | 431 | 760 |
| H(3) | 397 | 747 | 798 |
| H(4) | 468 | 494 | 917 |
| H(5) | 641 | 749 | 932 |
| H(6) | 622 | 450 | 837 |
| H(7)*A* | 795 | 701 | 833 |
| H(7)*B* | 839 | 535 | 890 |
| H(8) | 766 | 556 | 688 |
| H(9) | 828 | 278 | 684 |
| H(10) | 627 | 192 | 708 |
| H(11) | 606 | 416 | 570 |
| H(12) | 415 | 186 | 585 |
| H(13) | 378 | 441 | 468 |
| H(14)*A* | 201 | 192 | 475 |
| H(14)*B* | 185 | 301 | 396 |
| H(15) | 159 | 543 | 468 |
| H(17) | 519 | 576 | 697 |
| H(18) | 600 | 810 | 675 |
| H(23)*A* | 756 | 503 | 1202 |
| H(23)*B* | 857 | 654 | 1227 |
| H(23)*C* | 819 | 431 | 1168 |
| H(26)*A* | 968 | 663 | 762 |
| H(26)*B* | 957 | 512 | 699 |
| H(26)*C* | 1007 | 506 | 812 |
| H(30)*A* | 938 | 128 | 982 |
| H(30)*B* | 873 | −45 | 947 |
| H(30)*C* | 991 | 10 | 923 |
| H(31)*A* | −46 | 463 | 492 |
| H(31)*B* | 0 | 284 | 498 |
| H(31)*C* | −29 | 385 | 409 |

parameters led to an $R$ value of 6·2%. At this stage, the O(24)–C(25) distance was really too short (1·28 Å). A difference Fourier series was calculated omitting C(25). Two sites appeared which were attributed to two equally occupied positions of C(25). After introduction of those two atomic sites with occupation factors of $\frac{1}{2}$, and isotropic $B$ values, we resumed the refinement by full-matrix least squares; the final $R$ was 5·1%.

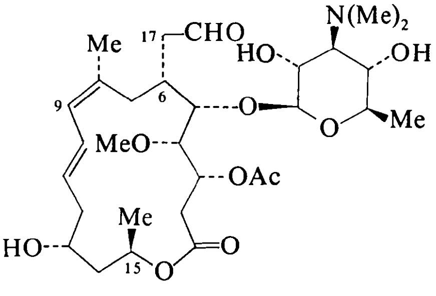
The atomic structure factors for C and O were taken from Doyle & Turner (1968), and for H from Stewart, Davidson & Simpson (1965). The atomic coordinates are listed in Table 1 for the heavy atoms, and in Table 2 for H. Bond distances and angles are presented in Tables 3 and 4.*



(I)



(II)



(III)

Table 3. *Intramolecular bond distances* (Å)

The e.s.d.'s, given in parentheses, refer to the last digit.

| | | | |
|---|---|---|---|
| C(1)–C(2) | 1·500 (5) | C(11)–C(12) | 1·459 (5) |
| C(1)–O(16) | 1·332 (5) | C(12)–C(13) | 1·324 (5) |
| C(1)–O(32) | 1·204 (5) | C(13)–C(14) | 1·473 (5) |
| C(2)–C(3) | 1·519 (5) | C(14)–C(15) | 1·513 (5) |
| C(3)–C(4) | 1·533 (4) | C(15)–O(16) | 1·458 (4) |
| C(3)–C(17) | 1·550 (5) | C(15)–C(31) | 1·489 (6) |
| C(4)–C(5) | 1·499 (5) | C(17)–C(18) | 1·497 (6) |
| C(4)–O(24) | 1·414 (4) | C(18)–O(19) | 1·082 (7) |
| C(5)–C(6) | 1·539 (4) | O(20)–C(21) | 1·344 (5) |
| C(5)–O(20) | 1·436 (4) | C(21)–O(22) | 1·188 (6) |
| C(6)–C(7) | 1·516 (5) | C(21)–C(23) | 1·481 (7) |
| C(6)–C(17) | 1·557 (4) | O(24)–C(25)*A* | 1·366 (10) |
| C(7)–C(8) | 1·526 (5) | O(24)–C(25)*B* | 1·379 (9) |
| C(8)–C(9) | 1·538 (5) | C(25)*A*–C(25)*B* | 0·991 (12) |
| C(8)–C(26) | 1·524 (5) | O(27)–C(28) | 1·332 (5) |
| C(9)–C(10) | 1·488 (5) | C(28)–O(29) | 1·194 (5) |
| C(9)–O(27) | 1·458 (4) | C(28)–C(30) | 1·493 (6) |
| C(10)–C(11) | 1·334 (5) | | |

Table 4. *Intramolecular bond angles* (°)

The e.s.d.'s, given in parentheses, refer to the last digit.

| | | | | | |
|---|---|---|---|---|---|
| C(2)–C(1)–O(16) | 110·8 (3) | C(6)–C(7)–C(8) | 119·0 (3) | C(1)–O(16)–C(15) | 118·7 (3) |
| C(2)–C(1)–O(32) | 124·8 (3) | C(7)–C(8)–C(9) | 115·2 (3) | C(3)–C(17)–C(6) | 104·7 (3) |
| O(16)–C(1)–O(32) | 124·4 (3) | C(7)–C(8)–C(26) | 108·9 (3) | C(3)–C(17)–C(18) | 110·7 (3) |
| C(1)–C(2)–C(3) | 114·0 (3) | C(9)–C(8)–C(26) | 110·1 (3) | C(6)–C(17)–C(18) | 112·3 (3) |
| C(2)–C(3)–C(4) | 113·4 (3) | C(8)–C(9)–C(10) | 116·4 (3) | C(17)–C(18)–O(19) | 132·7 (5) |
| C(2)–C(3)–C(17) | 112·5 (3) | C(8)–C(9)–O(27) | 105·9 (3) | C(5)–O(20)–C(21) | 117·7 (3) |
| C(4)–C(3)–C(17) | 105·5 (3) | C(10)–C(9)–O(27) | 109·1 (3) | O(20)–C(21)–O(22) | 123·2 (4) |
| C(3)–C(4)–C(5) | 104·7 (3) | C(9)–C(10)–C(11) | 126·0 (3) | O(20)–C(21)–C(23) | 111·4 (4) |
| C(3)–C(4)–O(24) | 111·8 (3) | C(10)–C(11)–C(12) | 124·4 (3) | O(22)–C(21)–C(23) | 125·4 (4) |
| C(5)–C(4)–O(24) | 111·4 (3) | C(11)–C(12)–C(13) | 125·3 (3) | C(4)–O(24)–C(25)*A* | 119·7 (4) |
| C(4)–C(5)–C(6) | 103·1 (3) | C(12)–C(13)–C(14) | 125·3 (3) | C(4)–O(24)–C(25)*B* | 115·7 (4) |
| C(4)–C(5)–O(20) | 110·5 (3) | C(13)–C(14)–C(15) | 115·0 (3) | C(9)–O(27)–C(28) | 117·2 (3) |
| C(6)–C(5)–O(20) | 112·4 (3) | C(14)–C(15)–O(16) | 106·6 (3) | O(27)–C(28)–O(29) | 124·1 (4) |
| C(5)–C(6)–C(7) | 114·9 (3) | C(14)–C(15)–C(31) | 114·0 (3) | O(27)–C(28)–C(30) | 111·2 (3) |
| C(5)–C(6)–C(17) | 99·9 (2) | O(16)–C(15)–C(31) | 107·8 (3) | O(29)–C(28)–C(30) | 124·7 (4) |
| C(7)–C(6)–C(17) | 119·4 (3) | | | | |

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* Lists of structure factors and thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32521 (17 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

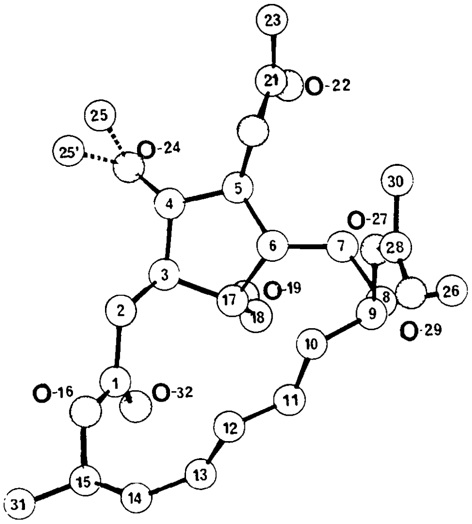

Fig. 1. The molecular structure of $C_{24}H_{34}O_8$.

Table 5. *Torsion angles* (°)

| | |
|---|---|
| (*a*) The macrocycle | |
| O(16)–C(1)–C(2)–C(3) | 169·2 |
| C(1)–C(2)–C(3)–C(4) | 179·6 |
| C(2)–C(3)–C(4)–C(5) | 140·4 |
| C(3)–C(4)–C(5)–C(6) | −40·2 |
| C(4)–C(5)–C(6)–C(7) | 176·0 |
| C(5)–C(6)–C(7)–C(8) | 177·8 |
| C(6)–C(7)–C(8)–C(9) | −56·2 |
| C(7)–C(8)–C(9)–C(10) | 75·3 |
| C(8)–C(9)–C(10)–C(11) | 56·0 |
| C(9)–C(10)–C(11)–C(12) | −177·3 |
| C(10)–C(11)–C(12)–C(13) | 165·4 |
| C(11)–C(12)–C(13)–C(14) | −174·0 |
| C(12)–C(13)–C(14)–C(15) | 107·0 |
| C(13)–C(14)–C(15)–O(16) | −59·8 |
| C(14)–C(15)–O(16)–C(1) | 99·2 |
| C(15)–O(16)–C(1)–C(2) | −165·8 |
| (*b*) The pentagonal cycle | |
| C(17)–C(3)–C(4)–C(5) | 16·8 |
| C(3)–C(4)–C(5)–C(6) | −40·2 |
| C(4)–C(5)–C(6)–C(17) | 47·0 |
| C(5)–C(6)–C(17)–C(3) | −35·9 |
| C(6)–C(17)–C(3)–C(4) | 12·6 |
| (*c*) The side chains | |
| H(4)–C(4)–O(24)–C(25)*A* | −24·2 |
| H(4)–C(4)–O(24)–C(25)*B* | 23·8 |
| H(5)–C(5)–O(20)–C(21) | 8·0 |
| C(5)–O(20)–C(21)–O(22) | −16·7 |
| H(9)–C(9)–O(27)–C(28) | −30·1 |
| C(9)–O(27)–C(28)–O(29) | 1·0 |
| H(17)–C(17)–C(18)–O(19) | 29·0 |

Table 6. *Deviations* (Å) *from the least-squares planes with reference to the orthogonal axes a, b and c**

Plane I: $0{\cdot}4143X - 0{\cdot}6988Y - 0{\cdot}5831Z + 5{\cdot}2156 = 0$.
Plane II: $0{\cdot}4603X - 0{\cdot}7276Y - 0{\cdot}5087Z + 4{\cdot}4011 = 0$.
Plane III: $0{\cdot}3615X - 0{\cdot}6454Y - 0{\cdot}6729Z + 5{\cdot}7729 = 0$.

| | Plane I | Plane II | Plane III |
|---|---|---|---|
| C(9) | −0·10 | 0 | −0·51† |
| C(10) | −0·01 | 0 | −0·40† |
| C(11) | 0·10 | 0 | −0·12† |
| C(12) | 0·13 | −0·06† | 0 |
| C(13) | −0·01 | −0·33† | 0 |
| C(14) | −0·11 | 0·51† | 0 |

Angle II, III = 12°.

† Atom not included in the calculation of the mean plane.

**Discussion.** (3,6)Bicycloleucomycin $A_3$ (I) was obtained (Ōmura, Nakagawa, Suzuki & Hata, 1974) from leucomycin $A_3$, a basic macrolide antibiotic produced by *Streptomyces kitasatoensis* Hata. The configurations at C(3), C(6) and C(17) of this compound were unknown, as was the configuration at C(9). The C(9) configuration was also an unsolved problem for leucomycin $A_3$ itself, as it could not be deduced from a previous X-ray investigation of demycarosyl leucomycin $A_3$ hydrobromide (Hiramatsu, Furusaki, Noda, Naya, Tomiie & Nitta, 1970) (III). The present X-ray structure analysis was performed on (II), which is the diacetyl derivative of the aglycone part of (I) (Ducruix, Pascard, Nakagawa & Ōmura, 1976).

Fig. 1 represents the macrocyle. C(25) occupies two positions: C(25)*A* and C(25)*B*. A list of the different torsion angles is given in Table 5. The five-membered ring is a twisted half-chair: $\Delta = 7°$, $\varphi = 47°$ (Altona, Geise & Romers, 1968). The plane defined by C(9), C(10), C(11) and C(12), and that containing C(12), C(13) and C(14) form an angle of 12° (Table 6).

By relating the established configuration of the title compound to the admitted absolute configuration of demycarosyl leucomycin hydrobromide (Hiramatsu *et al.*, 1970), an absolute configuration can be attributed to all the asymmetric centres: 3(*R*), 5(*S*), 6(*R*), 8(*R*), 9(*R*), 15(*R*), 17(*R*).

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