hydroxide. The resulting colorless precipitate was extracted with methylene chloride (3 × 25 mL), dried (Na_2SO_4), and evaporated to dryness to give the *N*-methyl-14-hydroxymorphinan as a colorless solid in high yield (>90%). Recrystallization from ethanol gave material with the following: mp 161.5–163 °C; NMR ($CDCl_3$) 1.8–3.8 (m with s at 2.3, 15), 5.70–5.90 (m, 2), 6.90–7.20 (m, 4.8); IR 3700–3350 cm^{-1}; UV, only end absorption with a shoulder at 215 nm; mass spectrum, *m/e* 255 (parent).

Acknowledgment. Generous financial help from the National Institute of Drug Abuse under Grant No. 5-R01-DA00534 is gratefully acknowledged. Additional support for this project was provided by BRSG S07 RR07105 awarded by the Biomedical Research Support Grant Program, Division of Research Resources, National Institutes of Health.

Registry No. 2 (R = H), 80879-09-0; **3**, 80879-10-3; **4**, 80879-11-4; **5**, 80879-12-5; **6**, 80879-13-6; **7**, 80879-14-7; **8**, 80879-15-8; **9**, 80879-16-9; *N*-methyl-14-hydroxymorphinan, 80879-17-0.

Crystal Structure and Stereochemistry of Amblyodiol[1]

Werner Herz*

Department of Chemistry, Florida State University, Tallahassee, Florida 32306

John F. Blount

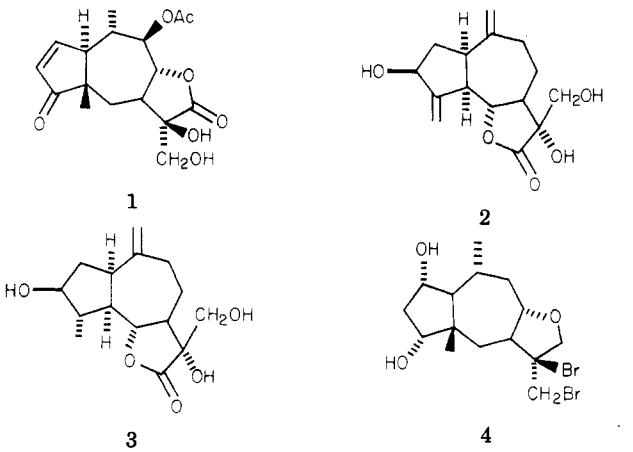
Research Division, Hoffmann-La Roche Inc., Nutley, New Jersey 07110

Received November 6, 1981

The helenanolide amblyodiol from *Gaillardia amblyodon*[2] is one of a small group of sesquiterpene lactones in which the ubiquitous α-methylene γ-lactone function is oxidized to an 11,13-diol.[3] The stereochemistry of such diol functions is difficult to determine unambiguously by chemical and spectroscopic methods. In the case of amblyodiol the relative and absolute stereochemistry shown in formula 1 (Chart I) for C-1, C-5, C-6, C-7, C-8, C-9, and C-10 has been established,[2] but attempts to use various CD methods[4] for solving the stereochemistry at C-11 failed,[2] and the results of solvent shift studies remained somewhat questionable.

To settle the stereochemistry at C-11 and to continue our study of the conformations of different types of sesquiterpene lactones, we undertook an X-ray analysis of amblyodiol. Crystal data for the substance are listed in the Experimental Section. Figure 1a is a stereoscopic drawing of the molecule which shows that the C-11 hydroxyl group is β and that our earlier[2] stereochemical assignments for the other asymmetric centers were correct. Figure 1 also represents the absolute configuration because of the negative Cotton effect due to the cyclopentenone chromophore.

Chart I



1 2 3 4

Table V. Torsion Angles (in Degrees) in 1 with Standard Deviations in Parentheses

C(1)-C(5)-C(6)-C(7)	35.8 (8)
C(5)-C(6)-C(7)-C(8)	38.8 (7)
C(6)-C(7)-C(8)-C(9)	−84.4 (6)
C(7)-C(8)-C(0)-C(10)	66.6 (8)
C(8)-C(9)-C(10)-C(1)	−47.8 (8)
C(0)-C(10)-C(1)-C(5)	69.2 (8)
C(10)-C(1)-C(5)-C(6)	−86.7 (8)
O(2)-C(8)-C(7)-C(11)	32.6 (5)
C(8)-C(7)-C(11)-C(12)	−33.2 (6)
C(7)-C(11)-C(12)-O(2)	23.2 (6)
C(11)-C(12)-O(2)-C(8)	−2.5 (6)
C(12)-O(2)-C(8)-C(7)	−19.5 (5)
C(1)-C(2)-C(3)-C(4)	1.6 (11)
C(2)-C(3)-C(4)-C(5)	13.8 (10)
C(3)-C(4)-C(5)-C(1)	−22.2 (8)
C(4)-C(5)-C(1)-C(2)	21.9 (8)
C(5)-C(1)-C(2)-C(3)	−15.5 (10)

Tables I–IV listing final atomic and final anistropic thermal parameters, bond lengths, and bond angles are available as supplementary material. Table V lists selected to torsion angles. As is apparent from these and also from Figure 1a and the framework model of Figure 1b, the cycloheptane ring is a twist chair whose twofold axis of symmetry passes through C-6 and the midpoint of the C-9,C-10 bond. Σ_2, the deviation of the ring from C_2 symmetry[5], is only 8°. The two five-membered rings are attached to the cycloheptane ring in the C-5(e), C-1(e) and the C-7(e), C-8(e) positions, respectively. The cyclopentenone is an envelope with C-5 as the flap, and the γ-lactone ring is also an envelope with C-7 as the flap.

The conformation of the cycloheptane ring of amblyodiol seems to be characteristic of helenanolides with a trans lactone ring closed to C-8.[6-8] Amblyodiol and the guaianolide 11,12-triols solstitialin (**2**)[3a] and cynaratriol (**3**)[3c] all have the same *absolute configuration* (*R*) at C-11, although the *orientation* of the 11-hydroxyl group of amblyodiol is opposite that found in **2** and **3** as the result of lactonization

(1) Work at the Florida State University was supported in part by a grant from the U.S. Public Health Service (CA-13121) through the National Cancer Institute.

(2) Herz, W.; Srinivasan, A. *Phytochemistry* **1974**, *13*, 1187.

(3) E.g. (a) solstitialin: Thiessen, W. E.; Hope, H.; Zarghani, N.; Heinz, D. E.; Deuel, P.; Hahn, E. A. *Chem. Ind. (London)* **1969**, 460. Thiessen, W. E.; Hope, H. *Acta Crystallogr., Sect. B* **1970**, *26*, 554. (b) Florigrandin and hymenoflorin: Herz, W.; Aota, K.; Hall, A. L.; Srinivasan, A. *J. Org. Chem.* **1974**, *39*, 2013. (c) Cynaratriol: Bernhard, H. O.; Thiele, K.; Pretsch, E. *Helv. Chim. Acta* **1979**, *62*, 1288.

(4) (a) Harada, N.; Nakanishi, K. *J. Am. Chem. Soc.* **1969**, *91*, 3989. Koreeda, M.; Harada, N.; Nakanishi, K. *Chem. Commun.* **1968**, 548. (b) Nakanishi, K.; Dillon, J. *J. Am. Chem. Soc.* **1971**, *93*, 4058. Nakanishi, K.; Schooley, D. A.; Koreeda, M.; Dillon, J. *Chem. Commun.* **1971**, 1235.

(5) McPhail, A. T.; Sim, G. A. *Tetrahedron* **1973**, *29*, 1751.

(6) Mazhar-ul-Haque; Rogers, D.; Caughlan, C. N. *J. Chem. Soc., Perkin 2* **1974**, 223.

(7) Sekita, T.; Inayama, S.; Iitaka, Y. *Tetrahedron Lett.* **1970**, 135.

(8) Inayama, S.; Ohkura, T.; Iitaka, Y. *Chem. Pharm. Bull.* **1977**, *25*, 1928.

0022-3263/82/1947-1594$01.25/0

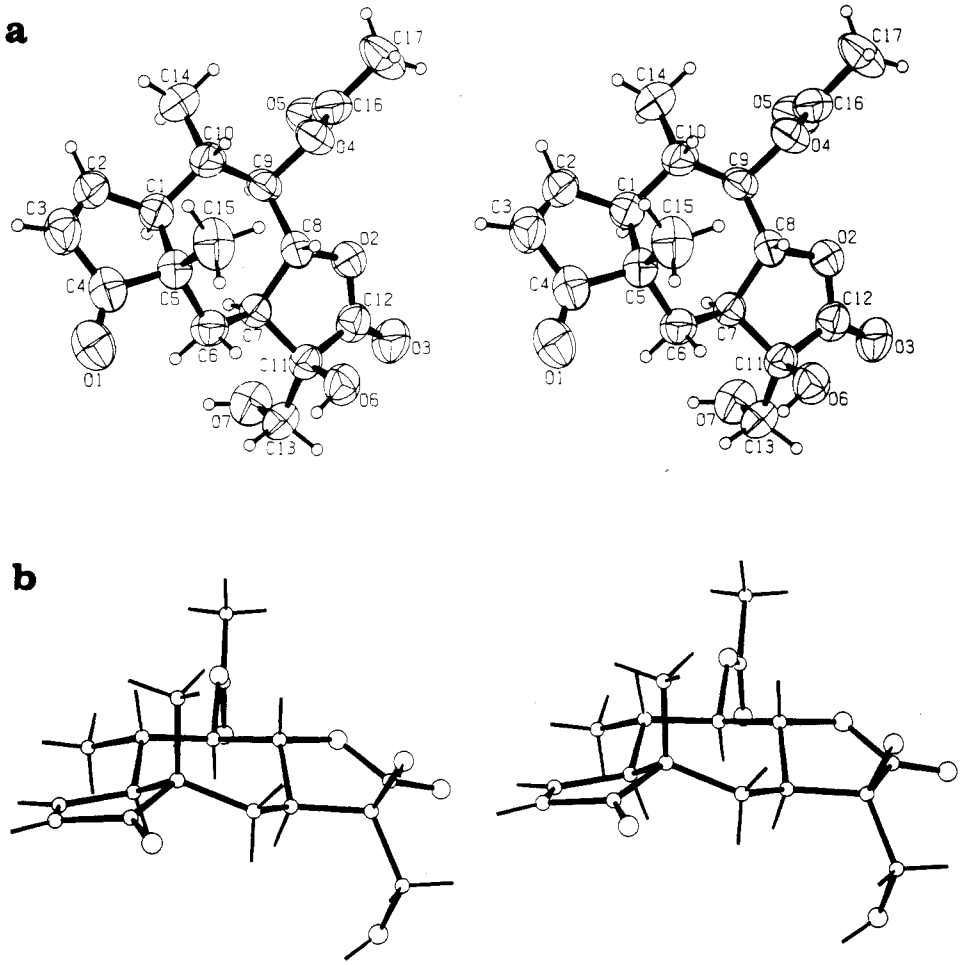


Figure 1. (a) Stereoscopic view of amblyodiol molecule with ellipsoids of thermal motion. (b) Side view of molecular framework.

toward C-8 rather than C-6. In the case of amblyodiol the C-11 stereochemistry can be rationalized by invoking enzymatic hydroxylation from the less hindered β side of an 11,13-unsaturated amblyodiol precursor in the manner in which bromination of pulchellin yields the dibromide4.[7]

Experimental Section

Single crystals of amblyodol were prepared by slow crystallization from ethyl acetate–hexane. The crystals were trigonal, space group $P3_2$ (for the configuration shown) or $P3_1$, with a = 9.682 (2) Å, c = 15.549 (6) Å, and d_{calcd} = 1.335 g cm^{-3} for Z = 3 ($C_{17}H_{22}O_7$, M_r = 338.36). The intensity data were measured on a Hilger-Watts diffractometer (Ni-filtered Cu Kα radiation, θ–2θ scans, pulse-height discrimination). The size of the crystal used for data collection was approximately 0.25 × 0.25 × 0.5 mm. A total of 1551 accessible reflections were measured for $\theta < 70°$, of which 1397 were considered to be observed [$I > 2.5\sigma(I)$]. The structure was solved by a multiple-solution procedure[9] and was refined by full-matrix least-squares methods. In the final refinement anisotropic thermal parameters were used for the nonhydrogen atoms, and isotropic temperature factors were used for the hydrogen atoms. The hydrogen atoms were included in the structure factor calculations, but their parameters were not refined. The final discrepancy indices are R = 0.054 and R_w = 0.062 for the 1397 observed reflections. The final difference map has no peaks greater than 0.4 eÅ^{-3}.

Supplementary Material Available: Tables I–IV listing final atomic parameters, final anisotropic thermal parameters, bond lengths, and bond angles for compound 1 (4 pages). Ordering information is given on any current masthead page.

(9) Germain, G.; Main, P.; Woolfson, M. M. *Acta Crystallogr. Sect. A* 1971, *A27*, 368.

Synthesis of 10,11-Anhydroerythromycin

J. R. Hauske* and G. Kostek

Pfizer Central Research, Groton, Connecticut 06340

Received November 9, 1981

In the course of investigating synthetic modifications of the erythromycin aglycon fragment, we desired the 10,11-anhydro derivative **1**. Although there is a novel synthetic route[1] to **1**, it requires a masking–unmasking sequence of the 2′-hydroxyl as well as the 4″-hydroxyl functions which is time consuming; also, it substantially decreases the overall yield.

Our synthetic analysis was based upon the projection that it should be possible to *selectively* introduce an electron-stabilizing functionality at the 11,12-position. This moiety would then be subjected to base-catalyzed elimination. In principle, 11,12-cyclic carbonate **2** would fulfull our requirements. Thus, exposure of erythromycin (**3**) to ethylene carbonate in toluene does afford intermediate **2**,[2] and subsequent treatment of **2** with tetramethylguanidine in dimethoxyethane cleanly affords anhydro derivative **1** (Scheme I).

(1) J. Tadanier, J. Martin, R. Egan, A. Goldstein, R. Stanaszek, E. Hirner, and F. Fischer, *J. Org. Chem.*, **39**, 2495 (1974); J. Tadanier, J. Martin, A. Goldstein and E., Hirner, *ibid*, **43**, 2351 (1978).

(2) W. Slawinski, H. Bojarska-Dahlig, T. Glabski, I. Dziegielewska, M. Biedrzycki, and S. Naperty, *Recl. Trav. Chim. Pays-Bas*, **94**, 236 (1975); H. W. Murphy, V. C. Stephens, and J. Conine, *U.S.* Patent 3417077 (1968); H. Bojarska-Dahlig and W. Slawinski, *Rocz.* Chem., **46**, 221 (1972).

0022-3263/82/1947-1595$01.25/0