

MICROBIAL PRODUCTS
VII. THE RELATIVE CONFIGURATION
OF ACTINOMYCETE METABOLITE
X-14881D

J. F. BLOUNT, D. N. GREELEY, H. MAEHR*,
A. PERROTTA, R. G. PITCHER, L. TODARO
and T. H. WILLIAMS

Roche Research Center, Hoffmann-La Roche Inc.,
Nutley, New Jersey 07110, U.S.A.

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We have recently described five derivatives of benz[a]anthracene as metabolites of actinomyces sp. X-14881.¹⁾ Four of these, namely components X-14881A~D, are optically active with 5, 5, 1 and 6 chiral centers, respectively. In view of their chemical similarity and the availability of a crystal structure analysis of component X-

14881A, the relative configurations were also assigned to components X-14881B, the recently synthesized²⁾ X-14881C, and, in part, X-14881D.

Although the ¹H and ¹³C NMR spectra were analyzed in considerable detail, the stereochemical analysis of the H3-H4 dihedral angle, a requirement for the determination of the total relative configuration of X-14881D (1), proved to be problematic.

Correlated homonuclear ¹H-¹H 2D NMR spectroscopy (COSY) of 1, using the HOMCOR pulse sequence, provided the spectrum (Fig. 1) as a contour plot. Starting from the top left-hand corner and proceeding along the diagonal, a 9-point square pattern reveals the ABX character of the aromatic H10, 11 and 9, and a 4-point square pattern the AB character of the olefinic H6 and 5. The next point on the diagonal, attributed to 12-OH, is part of a square connecting to H12 which, in turn, is part of a square connecting to H12a. This 3-spin pattern

Fig. 1.

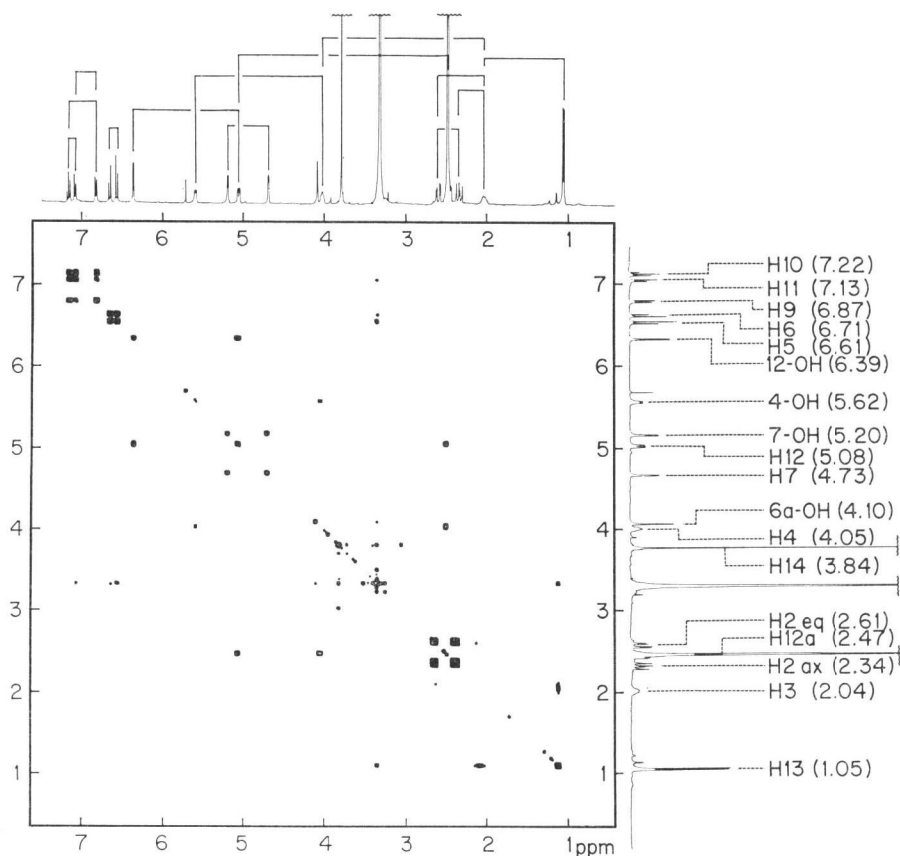
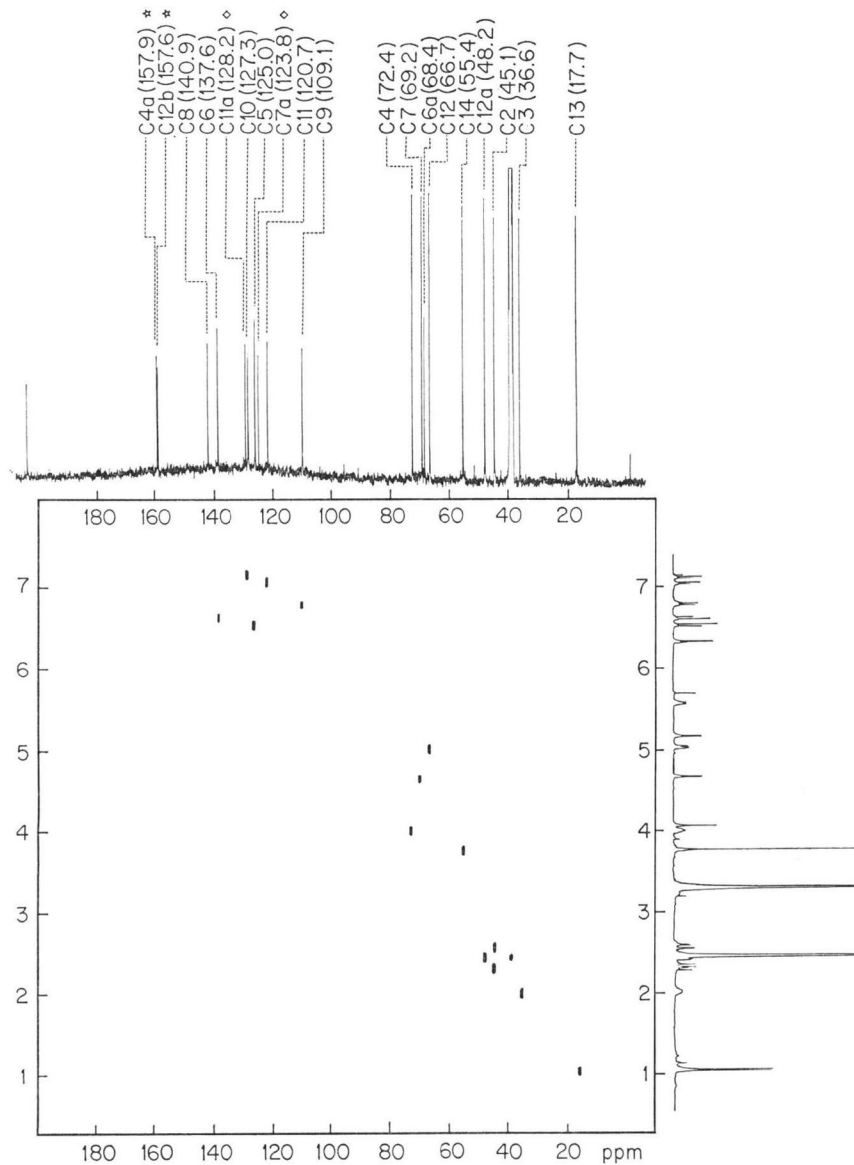


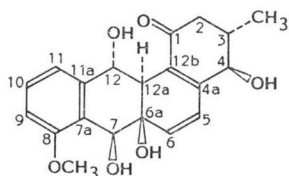
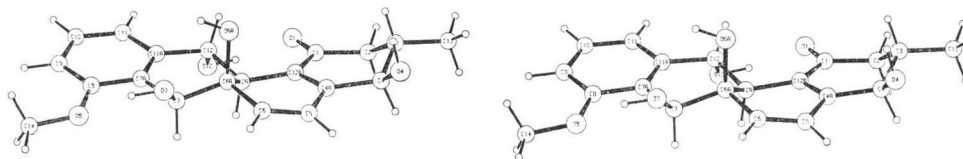
Fig. 2.



represents a AMX case without observed J_{ax} . The 4-OH at δ 5.62 is correlated to H4, which is further correlated to H12a *via* long-range interaction. A square centered at δ 4.97 correlates 7-OH and H7 as an AB case. The 6a-OH and the 9-OMe show no observed correlation. The next significant pattern is a pronounced square attributed to the anisochronous H2 methylene group correlated to H3 *via* $J_{2eq,3}$. Further, H3 is correlated to 3-Me. The only off-diagonal points not observed in this plot is the H3-H4 interaction.

Correlated heteronuclear ^1H - ^{13}C 2D NMR spectroscopy of **1**, employing the HETCOR pulse sequence, furnished the spectrum shown in Fig. 2. Of the 20 carbon peaks, two Me, one CH_2 , and 10 CH carbons are correlated with corresponding protons, thereby allowing unequivocal assignments. The quaternary carbons at 68.4, 140.9 and 201.1 ppm were unambiguously assigned to the C6a, C8 and carbonyl carbon C1, respectively. The remaining two pairs C4a, C12b and C7a, C11a, were attributed to olefin and aromatic carbons, respectively. The

Fig. 3. Stereoscopic drawing of one of the two independent molecules in the crystal of **1**.



X-14881D (**1**)

star and diamond symbols associated with these peaks (Fig. 2) denote possible interchange of the corresponding signals.

The relative configuration of **1** was finally solved by a single-crystal Roentgen diffraction analysis.

Component X-14881D, $[\alpha]_D^{25} +173^\circ$ (c 0.4, EtOH), crystallized from acetone-dichloromethane as prisms with space group $P2_1$, $a = 8.914(2)$, $b = 23.443(7)$, $c = 8.757(3)$ Å, $\beta = 109.11(2)^\circ$, and $d_{\text{calcd}} = 1.337$ g/cm³ for $Z = 4$. One pair of the four unit-cell molecules is not related to the other by crystallographic symmetry, but both pairs show very similar conformations. The stereo-drawing in Fig. 3 represents the conformation of one molecule in the crystal.

Since the effects of the anomalous scattering of oxygen were not sufficiently pronounced in the Friedel-pairs intensity data or in the final R-values of the refinements of the enantiomers, it was impossible to establish the absolute configuration of **1**. Consequently, the molecular drawing of **1** is shown with geometric descriptors³⁾ representing $[3R-(3\alpha,4\beta,6a\beta,7\beta,12\alpha,12a\alpha)]$ - or $[3S-(3\beta,4\alpha,6a\alpha,7\alpha,12\beta,12a\beta)]$ -3,4,6a,7,12,12a-hexahydro-4,6a,7,12-tetrahydroxy-8-methoxy-3-methylbenz[a]anthracen-1(2H)-one.

The size of the crystal used for data collection was approximately $0.40 \times 0.45 \times 0.5$ mm; the data (Hilger-Watts diffractometer, Ni-filtered Cu $K\alpha$ radiation, $\theta \sim 2\theta$ scans, pulse-height discrimination) were not corrected for absorption. Of the 2403 independent reflections for $\theta < 57^\circ$, 2372

were considered to be observed [$I > 2.5\sigma(I)$]. The structure was solved by a multiple-solution procedure⁴⁾ and was refined by block-diagonal least squares in which the matrix was partitioned into two blocks. Eight reflections which were strongly affected by extinction were excluded from the final refinement and difference map. 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 $R = 0.034$ and $wR = 0.047$ for the remaining 2364 observed reflections. The final difference map has no peaks greater than ± 0.2 eÅ⁻³.

The final atomic parameters, the final anisotropic thermal parameters, bond lengths and bond angles of metabolite X-14881D were deposited at the Crystallographic Data Center.

References

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