

## Fungal Metabolites. Part VI.<sup>1</sup> Crystal and Molecular Structure of Secalonic Acid A

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X-Ray analysis of secalonic acid A ( $C_{32}H_{30}O_{14} \cdot 2CH_3CO_2H$ ) has confirmed the 2,2'-nature of the biphenyl linkage between the two halves of the molecule. Together with the known stereochemistry at C(6), C(6') (I), this provides the absolute configuration of the molecule. The analysis has also indicated how the acetic acid molecules are incorporated in the crystal structure by hydrogen bonding. Estimation by n.m.r. of the torsion angle between adjacent C-OH and C-Me groups in secalonic acid A from solvent-induced changes of chemical shift was confirmed by the X-ray results.

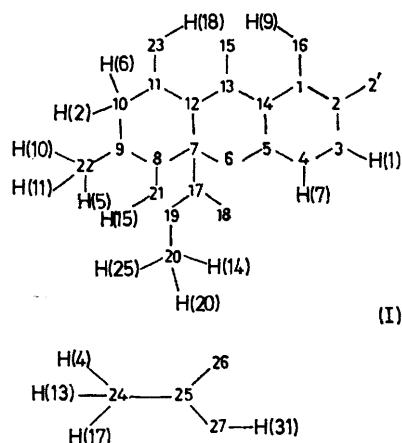
THE structure originally suggested for secalonic acid A (I) was one in which the biphenyl linkage between the

<sup>1</sup> Part V. A. W. Dunn, I. D. Entwistle, and R. A. W. Johnstone, *Phytochemistry*, 1975, **14**, 2081.

two halves of the molecule was 4,4', based mainly on dubious colour tests.<sup>2</sup> Subsequent careful analysis by

<sup>2</sup> For leading references see, B. Franck and E. M. Gottschalk, *Angew. Chem. Internat. Edn.*, 1964, **3**, 441.

n.m.r. of the chemical shifts for protons in secalonic acids, related compounds, and model compounds led to the structure assignment being modified to have a 2,2'-biphenyl linkage.<sup>3</sup> Recently we isolated the known



secalonic acid A and a new one (E)<sup>4</sup> from a fungal source different from those used in previous investigations. These secalonic acids were obtained with solvent of crystallisation (acetic acid, methanol, methylene chloride, or chloroform) held in molar ratios. Solvent was not removed on drying at 100 °C and 0.5 mmHg for 24 h and crystals isolated from different solvent had identical m.p.s; that the solvents had not reacted chemically was ascertained by n.m.r. spectroscopy. These properties are characteristic of clathrates. We undertook the X-ray analysis firstly to confirm the 2,2'-biphenyl linkage and secondly to determine how the solvent molecules were held in the crystal. Analysis<sup>5,6</sup> of solvent-induced changes of chemical shifts suggested that the torsional angle between C(5)-OH and C(6)-Me was  $90 \pm 11^\circ$  and it was of interest to know whether X-ray analysis of the structure would confirm this prediction in such a complex molecule.

#### EXPERIMENTAL

Secalonic acid A crystallises from acetic acid as yellow needles, m.p. 208–209 °C, elongated in the *b* direction.

**Crystal Data.**— $C_{32}H_{30}O_{14} \cdot 2CH_3CO_2H$ ,  $M = 758.7$ , monoclinic,  $a = 17.561(2)$ ,  $b = 7.185(1)$ ,  $c = 13.891(1)$ ,  $\beta = 91.11(1)$ ,  $U = 1752 \text{ \AA}^3$ ,  $D_m 1.42 \text{ g cm}^{-3}$ ,  $Z = 2$ ,  $D_o 1.438 \text{ g cm}^{-3}$ . Space group  $C2$  from systematic absences. Mo- $K_\alpha$  radiation,  $\lambda = 0.71069 \text{ \AA}$ ;  $\mu$  (Mo- $K_\alpha = 2.5 \text{ cm}^{-1}$ ).

**Crystallographic Measurements.**—Oscillation and Weissenberg photographs were taken about the *b* axes and the cell dimensions so obtained were refined to the values quoted on a Hilger-Watts four-circle diffractometer. Intensity measurements were made on the diffractometer by use of Mo- $K_\alpha$  radiation to  $\theta 30^\circ$  with the  $2\theta-\omega$  scan method. Of 2745 reflections measured, 2022 with a net count  $I > 3\sigma(I)$  were considered observed.

\* See Notice to Authors No. 7 in *J.C.S. Perkin I*, 1975, Index issue.

<sup>3</sup> J. W. ApSimon, J. A. Corran, N. G. Creasy, W. Marlow, W. B. Whalley, and K. Y. Sim, *J. Chem. Soc.*, 1965, 4144.

<sup>4</sup> C. C. Howard and R. A. W. Johnstone, *J.C.S. Perkin I*, 1973, 2440.

**Structure Analysis.**—The structure was solved by direct methods with MULTAN,<sup>7</sup> but only after considerable difficulty. Eventually, it was recognised that the partial structure revealed by the more promising *E* map was displaced from its true position relative to the two-fold axis on which the molecule lies. Development of the complete structure was further hindered by the pseudo-mirror symmetry arising from the near-equality of the majority of the *y* co-ordinates. However, when the correct structure was finally deduced, refinement by least-squares proceeded very satisfactorily. All hydrogen atoms were located from difference maps. The final refinements were by least-squares with the variables subdivided into five blocks, with hydrogen atoms refined isotropically and the heavier atoms anisotropically. The weighting scheme used was of the form  $w = 1$  when  $|F_o| < A$  and  $w = (|F_o|/A)^2$  when  $|F_o| > A$ , where  $A = 20.0$ . The final conventional *R* was 4.2% for all reflections. Thermal parameters and structure factors have been deposited in Supplementary Publication No: SUP 21729 (2 pp.)\*

#### RESULTS AND DISCUSSION

Bond lengths and angles are shown in Figure 1 and atom co-ordinates in the Table. The numbering of the atoms in Figure 1 is not systematic and does not cor-

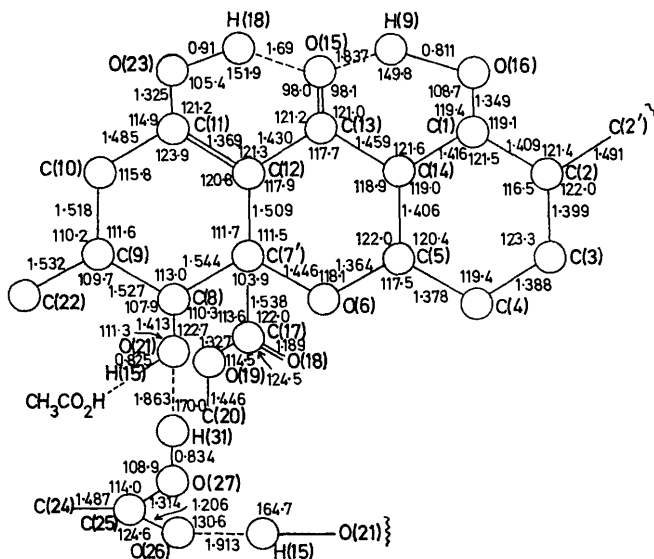


FIGURE 1 The asymmetric unit, showing bond length (Å) and angles (°), and crystallographic atom numbering system. Calculated  $\sigma$  for distances between heavier atoms 0.003–0.005 Å with the exception of bond C(24)–C(25) where it is 0.007 Å. Calculated  $\sigma$  of corresponding angles 0.2–0.3°. Dimensions involving hydrogen have calculated  $\sigma$  ca. ten times these values

respond with the carbon-atom numbering in formula (I).

The analysis confirms the structure (I) for secalonic acid A, and taken together with the known *R*-centres at C(6) and C(6') (I), gives the absolute configuration of the

<sup>5</sup> C. C. Howard and R. A. W. Johnstone, *J.C.S. Perkin II*, 1974, 1583.

<sup>6</sup> P. V. Demarco, E. Farkas, D. Doddrell, B. L. Mylari, and E. Wenkert, *J. Amer. Chem. Soc.*, 1968, **90**, 5480.

<sup>7</sup> G. Germain, P. Main, and M. M. Woolfson, *Acta Cryst.*, 1971, **A27**, 368.

molecule. The angle between the planes of the benzene rings comprising the 2,2'-biphenyl linkage is  $36.5^\circ$ . The torsional angle between C(5)-OH and C(6)-Me is  $92^\circ$ , in excellent agreement with the prediction ( $90 \pm 11^\circ$ ) based

Fractional atomic co-ordinates ( $\times 10^3$  for H;  $\times 10^4$  for C, O) with estimated standard deviations in parentheses for half the molecule

Atom	<i>x</i>	<i>y</i>	<i>z</i>
C(1)	1 070(1)	4 539(3)	64(2)
C(2)	327(1)	4 988(3)	351(2)
C(3)	247(1)	5 555(4)	1 307(2)
C(4)	853(1)	5 684(4)	1 959(2)
C(5)	1 574(1)	5 216(4)	1 668(2)
C(6)	2 185(1)	5 425(3)	2 321(1)
C(7)	2 862(1)	4 442(4)	2 152(2)
C(8)	3 451(1)	5 448(4)	2 806(2)
C(9)	4 271(1)	4 887(4)	2 600(2)
C(10)	4 454(1)	5 126(4)	1 544(4)
C(11)	3 821(1)	4 721(4)	850(2)
C(12)	3 076(1)	4 530(4)	1 106(2)
C(13)	2 478(1)	4 406(4)	396(2)
C(14)	1 698(1)	4 637(4)	717(2)
O(15)	2 623(1)	4 222(4)	-401(1)
O(16)	1 184(1)	4 017(3)	-854(1)
C(17)	2 794(1)	2 397(4)	2 466(2)
O(18)	3 317(1)	1 349(3)	2 429(2)
O(19)	2 106(1)	1 942(3)	2 767(2)
C(20)	2 032(2)	30(5)	3 076(4)
O(21)	3 314(1)	5 057(4)	3 784(1)
C(22)	4 822(2)	6 041(7)	3 226(3)
O(23)	4 020(1)	4 664(4)	-65(2)
C(24)	1 183(3)	4 230(8)	4 590(4)
C(25)	1 489(2)	6 083(5)	4 874(2)
O(26)	2 112(1)	6 651(4)	4 672(2)
O(27)	1 015(1)	7 097(6)	5 373(2)
H(1)	-27(1)	593(4)	151(2)
H(2)	460(2)	649(5)	142(2)
H(3)	338(2)	682(5)	273(2)
H(4)	59(3)	464(9)	438(4)
H(5)	472(3)	748(9)	309(4)
H(6)	490(2)	439(5)	137(2)
H(7)	78(2)	609(5)	260(2)
H(8)	435(2)	344(6)	282(2)
H(10)	475(2)	595(8)	389(3)
H(11)	530(2)	599(7)	303(3)
H(13)	141(3)	365(9)	399(4)
H(14)	247(3)	-23(9)	351(3)
H(15)	291(2)	551(5)	396(2)
H(17)	124(3)	348(9)	506(4)
H(18)	358(2)	442(6)	-40(2)
H(20)	148(3)	-16(9)	323(4)
H(25)	212(3)	-80(9)	255(4)
H(31)	124(2)	805(6)	557(2)

on n.m.r. measurements of solvent-induced changes in chemical shifts.<sup>4</sup> A perspective drawing of the secalonic acid A molecule is shown in Figure 2.

Crystals of secalonic acid A are composed of molecules stacked along *b*, with the stacks repeated along *a* to form sheets. These sheets are interleaved with sheets containing acetic acid. Each acetic acid molecule is involved in hydrogen bonding with two molecules of secalonic acid A, donating one hydrogen atom to the

C(5)-OH group of one molecule and accepting one hydrogen from the C(5')-OH of a second molecule in the next sheet. The hydrogen bonds thus formed compose

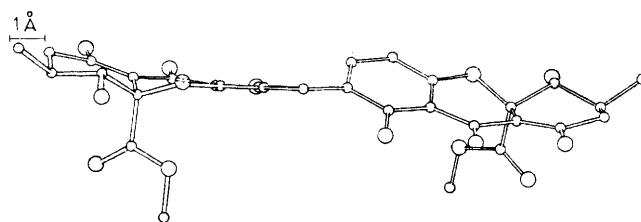


FIGURE 2 Perspective drawing of the molecules of secalonic acid A

infinite helices of hydrogen bonds which help hold the crystal together. This is seen in Figure 3 which shows the crystal structure in projection down *b*.

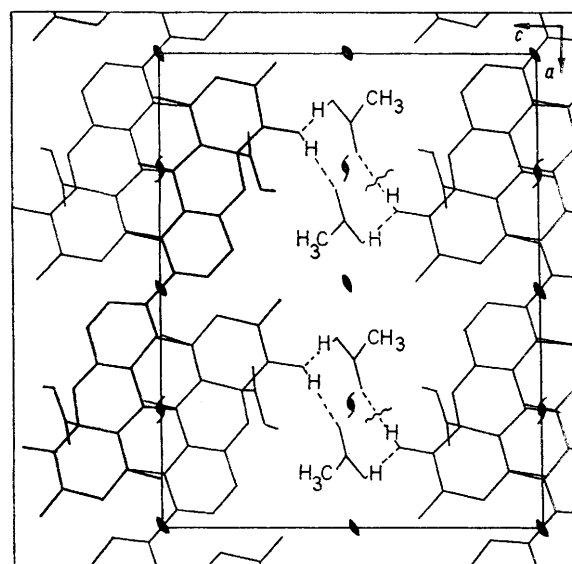


FIGURE 3 Projection of the unit cell down the *b* axis

The acetic acid in this crystal is clearly not held as in a clathrate structure, but rather is incorporated as solvent of crystallisation by means of a hydrogen-bond system of a common type. Such a hydrogen-bond system is clearly not possible when solvents such as chloroform are incorporated into crystals of secalonic acids. It thus seems unlikely that the crystal structures of secalonic acid A containing different solvents of crystallisation are all similar. Whether some are in fact true clathrates remains to be seen.

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