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Structure of Ergosterol-Biosynthesis Inhibitors. I. Structure of 1-(4-Fluorophenyl)-1-(3-pyridyl)-but-3-yn-1-ol, $C_{15}H_{12}FNO$

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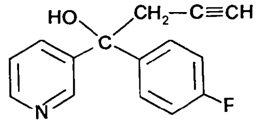
Abstract. $M_r = 241{\cdot}26$, monoclinic, $P2_1/c$, $a = 12{\cdot}609$ (6), $b = 7{\cdot}681$ (4), $c = 12{\cdot}645$ (6) Å, $\beta = 94{\cdot}97$ (2)°, $U = 1220{\cdot}05$ Å^3, $Z = 4$, $D_x = 1{\cdot}31$ g cm^{-3}, λ(Mo $K\bar{\alpha}$) = 0·71069 Å, $\mu = 0{\cdot}619$ cm^{-1}, $F(000) = 476$, room temperature, $R = 0{\cdot}064$ for 1232 observed reflections. The product, a new synthetic molecule showing some activity as an inhibitor of the biosynthesis of ergosterol in fungi, shows a quaternary central C and the presence of two aromatic rings, one containing N (pyridine). These rings are inclined at an angle of 84 (1·1)° to each other.

Introduction. The introduction of compounds which inhibit ergosterol biosynthesis in fungi is a recent development in the use of chemicals to control fungal diseases in plants (Siegel, 1981).

An interesting feature of these substances is that several classes of compounds, having different chemical structures, seem to share a similar mechanism of action: *e.g.* some triazoles (triadimefon, triadimenol), pyrimidines (fenarimol) and pyridines (buthiobate). It has been shown that these products cause an accumulation of [C(4) and C(14)] methylated sterols in fungal cells due to the inhibition of 14-methyl demethylase (Mercer, 1983).

The study of quantitative structure–activity relationships for one class of compounds (Krämer, Büchel, Meiser, Brandes, Haspers & Scheinpflug, 1979) has stressed the importance of steric requirements; we have therefore started a systematic structural study of some ergosterol inhibitors to look for possible similarities among them.

We report here the solid-state structure of a new compound (1) possessing some activity against fungal disease (Arnoldi, Betto, Ceresa, Farina, Formigoni, Galli & Scaglioni, 1983).



(1)

Experimental. White, transparent crystals with a prismatic habit and stable to air obtained by slow evaporation of an ethanolic solution; crystal of approximate dimensions 0·3 × 0·3 × 0·2 mm chosen for X-ray analysis; cell constants from counter data with a least-squares fitting of 2θ values of 25 high-angle reflections ($2\theta \geq 20°$); Philips PW 1100 diffractometer (graphite-monochromated Mo $K\bar{\alpha}$ radiation), $2\theta \leq 50°$, $\omega/2\theta$ scan, scan speed 0·05° s^{-1}, scan width 1·00°; two background counts measured at each side of the peaks for 5 s and values averaged; 2322 independent reflections of which 1232 considered observed by the criterion $I \geq 3\sigma(I)$ (based on counting statistics) and subsequently used for refinement, range of *hkl*: h −14→14, k 0→9, l 0→14; Lorentz and polarization corrections, no absorption or extinction correction; two standard reflections (110, $\bar{1}10$) measured every 60 min to check stability of crystal and experimental conditions, no significant variations detected.

Structure solved using *MULTAN*76 (Main, Lessinger, Woolfson, Germain & Declercq, 1976); E map calculated from set with highest figure of merit revealed all but the H atoms; refinement by block-diagonal least squares, anisotropic temperature factors for C, N, O and F atoms; H atoms in their idealized positions (C—H 1·080 Å) included and refined in last cycles of refinement, $\sum w(|F_o| - |F_c|)^2$ minimized with a Cruickshank weighting scheme (Cruickshank, 1970); final conventional $R = 0{\cdot}064$, $R_w = 0{\cdot}076$, $S = 2{\cdot}3$; $\Delta/\sigma = 0{\cdot}4$; final $\Delta\rho\,|\,0{\cdot}7\,|$ e Å^{-3}. Atomic scattering

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factors from *International Tables for X-ray Crystallography* (1974) and correction included for real part of anomalous dispersion.

Discussion. Final atomic coordinates and isotropic temperature factors are given in Table 1. Bond lengths and angles are shown in Table 2, some relevant torsion angles in Table 3.*

The conformation of the molecule (Fig. 1) is best described by looking at the internal rotation angles (see Table 3) C(5)–C(1)–C(11)–C(12) 80·1 (9), C(10)–C(5)–C(1)–C(11) 4·1 (9), O(1)–C(1)–C(11)–C(12) −158·4 (8) and O(1)–C(1)–C(2)–C(3) −121·0 (9)°. The angle between the pyridine ring and the benzene ring is 84 (1·1)°.

The distances from the tetrahedral carbon C(1) and the substituents are in the expected range (Sutton, 1958).

There is a slight distortion of the C(1)–C(5)–C(10) and C(1)–C(5)–C(6) angles [122·6 (4) and 118·7 (4)° respectively] possibly due to intramolecular steric interactions.

It may be expected that the presence of a substituent in the phenyl ring will cause some systematic deformation of its geometry (Domenicano, Vaciago & Coulson, 1975*a,b*).

There is no significant effect on the bond lengths at the level of the standard deviations obtained in this structure [av. value for the C–C bond length 1·38 (1) Å] but the angles [av. value 120·0 (2·4)°] show the expected trend. In fact the C(7)–C(8)–C(9) and C(6)–C(5)–C(10) angles [123·3 (5) and 118·7 (5)°] compare with the values of 123·4 and 118·1° reported in the literature (Domenicano, Mazzeo & Vaciago, 1976).

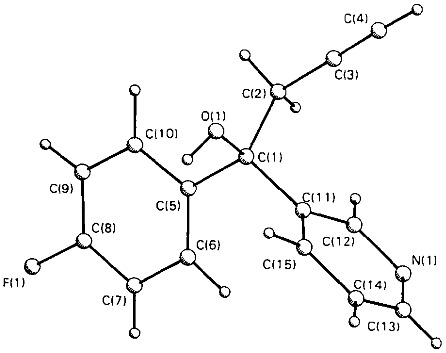

Fig. 1. A *PLUTO* view (Motherwell, 1978) of the molecule showing the atom-numbering scheme.

Table 1. *Final positional parameters (e.s.d.'s on the last significant figure in parentheses) and B values* (Å²) (*Willis & Pryor*, 1975)

$$B_{\rm eq} = \tfrac{8}{3}\pi^2\textstyle\sum_i\sum_j U_{ij}a^*_i a^*_j \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	$B_{\rm eq}/B$
N(1)	0·1185 (4)	0·6656 (7)	0·7482 (4)	3·79
F(1)	0·4846 (4)	0·3600 (7)	0·3337 (4)	6·42
O(1)	0·1990 (4)	0·9923 (6)	0·4396 (5)	3·47
C(1)	0·2462 (5)	0·8806 (8)	0·5210 (5)	2·54
C(2)	0·3223 (5)	0·9982 (9)	0·5910 (5)	3·32
C(3)	0·2685 (5)	1·1383 (9)	0·6428 (5)	3·77
C(4)	0·2280 (7)	1·2541 (10)	0·6860 (7)	5·51
C(5)	0·3087 (5)	0·7356 (8)	0·4699 (4)	2·69
C(6)	0·3948 (5)	0·7815 (9)	0·4138 (5)	3·57
C(7)	0·4538 (5)	0·6536 (11)	0·3680 (5)	4·28
C(8)	0·4245 (6)	0·4844 (10)	0·3779 (5)	4·07
C(9)	0·3410 (6)	0·4337 (10)	0·4310 (5)	4·31
C(10)	0·2837 (5)	0·5628 (8)	0·4786 (5)	3·21
C(11)	0·1613 (5)	0·8038 (8)	0·5869 (5)	2·68
C(12)	0·1883 (5)	0·7411 (9)	0·6888 (5)	3·41
C(13)	0·0183 (5)	0·6501 (9)	0·7083 (6)	3·99
C(14)	−0·0171 (5)	0·7106 (10)	0·6098 (6)	4·17
C(15)	0·0560 (5)	0·7895 (9)	0·5470 (5)	3·83
H(C1)	0·167 (5)	0·938 (8)	0·386 (5)	3 (1)
H(1C2)	0·363 (4)	0·919 (7)	0·646 (4)	3 (1)
H(2C2)	0·376 (4)	1·052 (7)	0·553 (4)	3 (1)
H(C4)	0·195 (8)	1·341 (14)	0·726 (8)	11 (3)
H(C6)	0·417 (5)	0·916 (9)	0·407 (5)	4 (2)
H(C7)	0·516 (4)	0·676 (7)	0·331 (4)	4 (1)
H(C9)	0·318 (5)	0·321 (8)	0·435 (5)	4 (2)
H(C10)	0·219 (4)	0·522 (7)	0·516 (4)	4 (1)
H(C12)	0·263 (5)	0·750 (8)	0·721 (5)	4 (1)
H(C13)	−0·033 (6)	0·602 (10)	0·746 (6)	6 (2)
H(C14)	−0·086 (8)	0·706 (13)	0·579 (8)	11 (3)
H(C15)	0·050 (5)	0·851 (9)	0·472 (5)	5 (2)

Table 2. *Bond distances* (Å) *and angles* (°) *with e.s.d.'s in parentheses*

C(1)–C(2)	1·541 (9)	C(11)–C(12)	1·390 (9)
C(2)–C(3)	1·458 (10)	C(11)–C(15)	1·383 (9)
C(3)–C(4)	1·182 (11)	C(13)–C(14)	1·367 (10)
C(1)–C(5)	1·538 (8)	C(14)–C(15)	1·405 (10)
C(1)–C(11)	1·531 (9)	N(1)–C(12)	1·338 (9)
C(5)–C(6)	1·393 (9)	N(1)–C(13)	1·324 (9)
C(5)–C(10)	1·370 (9)	O(1)–C(1)	1·430 (7)
C(6)–C(7)	1·388 (10)	F(1)–C(8)	1·369 (9)
C(7)–C(8)	1·359 (11)		
C(8)–C(9)	1·355 (11)	C–H[a]	0·98 (7)
C(9)–C(10)	1·393 (10)	O–H	0·86 (6)
C(1)–C(2)–C(3)	113·6 (5)	C(8)–C(9)–C(10)	117·6 (5)
C(1)–C(5)–C(6)	118·7 (4)	C(11)–C(15)–C(14)	119·0 (5)
C(1)–C(5)–C(10)	122·6 (4)	C(13)–C(14)–C(15)	118·9 (5)
C(2)–C(3)–C(4)	177·8 (4)	C(12)–N(1)–C(13)	118·5 (4)
C(2)–C(1)–C(5)	110·5 (4)	N(1)–C(12)–C(11)	123·4 (4)
C(2)–C(1)–C(11)	110·0 (4)	N(1)–C(13)–C(14)	122·8 (4)
C(5)–C(1)–C(11)	110·9 (4)	O(1)–C(1)–C(2)	105·2 (4)
C(6)–C(5)–C(10)	118·7 (4)	O(1)–C(1)–C(5)	109·2 (4)
C(5)–C(6)–C(7)	120·2 (5)	O(1)–C(1)–C(11)	110·8 (4)
C(5)–C(10)–C(9)	121·6 (4)	F(1)–C(8)–C(7)	117·8 (5)
C(6)–C(7)–C(8)	118·6 (5)	F(1)–C(8)–C(9)	118·9 (5)
C(7)–C(8)–C(9)	123·3 (5)		

(*a*) Average value; e.s.d. in parentheses refers to the estimated standard deviation of the mean.

Table 3. *Torsion angles* (°) (*the e.s.d.'s on the angles are in the range* 0·9–1·2°)

C(1)–C(2)–C(3)–C(4)	−174·1	C(3)–C(2)–C(1)–C(11)	−56·7
C(2)–C(1)–C(11)–C(12)	−42·5	N(1)–C(12)–C(11)–C(1)	−177·0
C(2)–C(1)–C(5)–C(6)	126·5	O(1)–C(1)–C(2)–C(3)	−121·0
C(5)–C(1)–C(11)–C(12)	80·1	O(1)–C(1)–C(11)–C(12)	−158·4
C(10)–C(5)–C(1)–C(11)	4·1	O(1)–C(1)–C(5)–C(6)	−118·3

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* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39724 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

There is one short intermolecular (2·81 Å) distance between the O atom and a symmetry-related (x, $1+y$, $1-z$) N of the pyridine ring, consistent with a hydrogen-bond interaction. The other packing distances are longer than 3·2 Å.

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Tétraméthyl-1,1′,3,3′ Biindène-1:1′-(±), $C_{22}H_{22}$

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Abstract. $M_r = 286$, orthorhombic, $Pna2_1$, $a = 12{\cdot}204\,(8)$, $b = 16{\cdot}854\,(12)$, $c = 7{\cdot}985\,(5)$ Å, $V = 1642{\cdot}4\,(19)$ Å^3, $Z = 4$, $D_x = 1{\cdot}2$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}71069$ Å, $\mu = 0{\cdot}32$ cm^{-1}, $F(000) = 616$, room temperature, $R = 0{\cdot}085$ for 839 reflections. The compound corresponds to the diastereoisomer (±), which exists in the two enantiomeric forms *S,S* and *R,R*. The indene groups are each planar with an angle of 120° between the planes. The molecules stack fairly compactly and are held together by van der Waals forces.

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Introduction. Nous avons entrepris depuis plusieurs années l'étude de la polymérisation par voie cationique des biindènes-1:1′ dont les polymères présentent des caractéristiques thermiques intéressantes puisque leur point de fusion est généralement supérieur à 620 K.

Le polybiindène-1:1′ est connu depuis les travaux de Maréchal, Basselier & Sigwalt (1964) mais le mécanisme de polymérisation demeurait obscur. Il a récemment été montré (Nicolet, Sanchez & Abadie, 1981) que le maillon majoritaire, dans ces polymères,