

17-Ethynyl-3,17 $\alpha$ -dimethoxy-5 $\beta$ -estra-1,3,5(10)-triene

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## Key indicators

Single-crystal X-ray study

$T = 293\text{ K}$

Mean  $\sigma(\text{C}-\text{C}) = 0.004\text{ \AA}$

$R$  factor = 0.058

$wR$  factor = 0.151

Data-to-parameter ratio = 10.3

For details of how these key indicators were  
 automatically derived from the article, see  
<http://journals.iucr.org/e>.

The title compound,  $\text{C}_{22}\text{H}_{28}\text{O}_2$ , was synthesized from 17 $\alpha$ -ethynylestradiol in 86% yield. The X-ray structure determination shows that, in the steroid nucleus, one of the cyclohexane rings adopts a half-chair conformation and the other shows a chair conformation. The cyclopentane ring adopts an envelope conformation. In the crystal structure, symmetry-related molecules exist as  $\text{C}-\text{H}\cdots\text{O}$  hydrogen-bonded dimers.

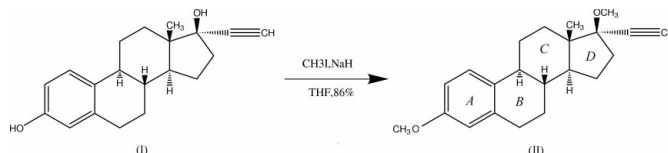
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## Comment

17 $\alpha$ -Ethynylestradiol, (I), was the first well known synthetic estrogen, first reported in 1938 (Inhoffen *et al.*, 1938). The role of monoethers of 17 $\alpha$ -ethynylestradiol, such as mestranol (Colton, 1954) and quinestrol (Ercoli & Gardi, 1961), is well established in oral contraception and these compounds are widely used in oral contraceptive pills and as antifertility agents (Greenblatt, 1967). This paper describes the synthesis of the title dimethyl ether, (II), of 17 $\alpha$ -ethynylestradiol and its structural elucidation through X-ray diffraction studies. Compound (II) was synthesized by methylation of (I) with methyl iodide and NaH under an inert atmosphere of argon gas in an excellent yield (86%).



Refinement of the Flack (1983) parameter failed to determine the absolute configuration of (II) due to the absence of heavy atoms. However, the L-enantiomer was chosen on the

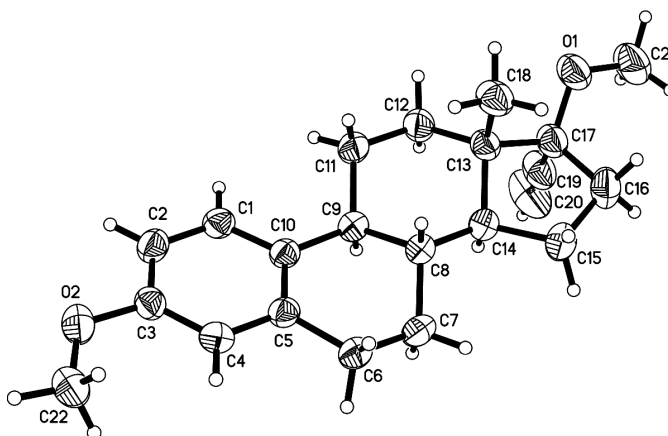
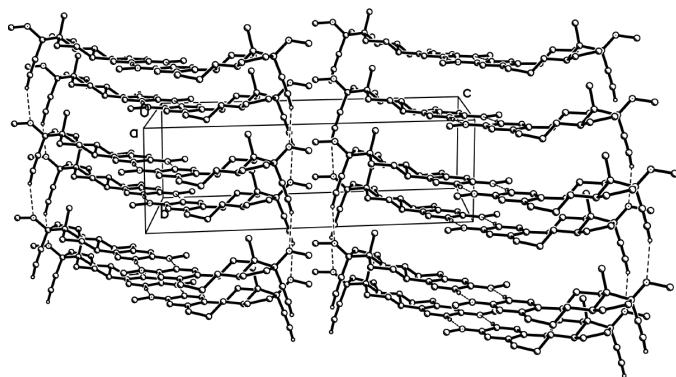


Figure 1

The structure of (II) showing 50% probability displacement ellipsoids and the atom-numbering scheme.



**Figure 2**  
A view of the molecular packing in (II). Only those H atoms involved in hydrogen bonding are shown.

basis of the absolute configuration of the starting material, (I), as compound (II) was obtained from (I) *via* a non-stereodestructive reaction.

The bond lengths and angles in (II) (Fig. 1) agree with those reported for 17 $\alpha$ -ethynylestradiol (van Geerestein, 1987). Ring A is planar to within  $\pm 0.012$  (3) Å. As observed for the estradiol structure, ring B has a half-chair conformation and ring C is in an ideal chair conformation; ring D adopts an envelope conformation (van Geerestein, 1987). In the steroid nucleus of (II), the B/C and C/D ring junctions are *trans*-fused. The methoxy substituent at the C3 position is twisted out of the plane of ring A [C2–C3–O2–C22 torsion angle  $-178.8$  (3) $^\circ$ ]. At the C17 position, the methoxy substituent is equatorially attached and the acetylenic substituent is axially oriented.

The molecular packing in (II) is illustrated in Fig. 2. In the crystalline state, the molecules at positions ( $x, y, z$ ) and ( $1 - x, y, -z$ ) are linked by C–H $\cdots$ O hydrogen bonds to form dimers (Table 2). These dimers are linked by C–H $\cdots$ O interactions to form molecular columns along the  $b$  axis.

## Experimental

NaH (123.2 mg, 3.08 mmol) was added to compound (I) (500 mg, 1.54 mmol) in tetrahydrofuran (30 ml, dried), followed by methyl iodide (0.2 ml, 3.08 mmol). The reaction mixture was stirred at room temperature under dry inert conditions for 2 h. After completion of the reaction, excess NaH was decomposed by adding a few drops of acetic acid. The solvent was evaporated and water (20 ml) was added to the reaction flask. The organic layer was extracted with dichloromethane (253 ml), and the combined organic layer was washed with water, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo* to yield compound (II) in 86.2% yield (431 mg). Compound (II) was recrystallized from petroleum ether–dichloromethane (1:2).

### Crystal data

C <sub>22</sub> H <sub>28</sub> O <sub>2</sub>	$D_x = 1.196 \text{ Mg m}^{-3}$
$M_r = 324.44$	Mo $K\alpha$ radiation
Monoclinic, C2	Cell parameters from 4503 reflections
$a = 12.340$ (2) Å	$\theta = 2.9\text{--}27.6^\circ$
$b = 6.8289$ (13) Å	$\mu = 0.07 \text{ mm}^{-1}$
$c = 21.710$ (4) Å	$T = 293$ (2) K
$\beta = 100.037$ (4) $^\circ$	Block, colourless
$V = 1801.4$ (6) Å <sup>3</sup>	$0.57 \times 0.51 \times 0.39 \text{ mm}$
$Z = 4$	

### Data collection

Siemens SMART CCD area-detector diffractometer	2221 independent reflections
$\omega$ scans	2141 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (SADABS; Sheldrick, 1996)	$R_{\text{int}} = 0.018$
$T_{\text{min}} = 0.959, T_{\text{max}} = 0.972$	$\theta_{\text{max}} = 27.6^\circ$
6003 measured reflections	$h = -16 \rightarrow 16$
	$k = -7 \rightarrow 8$
	$l = -28 \rightarrow 27$

### Refinement

Refinement on $F^2$	$w = 1/[\sigma^2(F_o^2) + (0.0874P)^2 + 0.3877P]$
$R[F^2 > 2\sigma(F^2)] = 0.058$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.151$	$(\Delta/\sigma)_{\text{max}} < 0.001$
$S = 1.20$	$\Delta\rho_{\text{max}} = 0.27 \text{ e } \text{Å}^{-3}$
2221 reflections	$\Delta\rho_{\text{min}} = -0.23 \text{ e } \text{Å}^{-3}$
216 parameters	
H-atom parameters constrained	

**Table 1**

Selected geometric parameters (Å,  $^\circ$ ).

O1–C17	1.415 (3)	O2–C22	1.412 (3)
O1–C21	1.425 (3)	C17–C19	1.469 (5)
O2–C3	1.368 (3)	C19–C20	1.156 (6)
C17–O1–C21	114.4 (3)	C20–C19–C17	177.4 (4)
C3–O2–C22	117.15 (18)	C21–O1–C17–C13	$-179.8$ (3)
C22–O2–C3–C4	1.6 (4)	C21–O1–C17–C16	66.7 (3)
C22–O2–C3–C2	$-178.8$ (3)		

**Table 2**

Hydrogen-bonding geometry (Å,  $^\circ$ ).

$D\text{--}H\cdots A$	$D\text{--}H$	$H\cdots A$	$D\cdots A$	$D\text{--}H\cdots A$
C2–H2 $\cdots$ O2 <sup>i</sup>	0.93	2.46	3.386 (3)	174
C20–H20 $\cdots$ O1 <sup>ii</sup>	0.93	2.53	3.415 (6)	159

Symmetry codes: (i)  $1 - x, y, -z$ ; (ii)  $x, 1 + y, z$ .

Atom H20 was located from a difference map and allowed to ride on its attached atom. The remaining H atoms were placed in calculated positions (C–H = 0.96–0.98 Å), with  $U_{\text{iso}} = 1.5U_{\text{eq}}$  of the parent atom for methyl H atoms and  $1.2U_{\text{eq}}$  (parent) for the remaining positions. The Friedel reflections were merged before the final refinement because of the absence of significant anomalous scattering effects.

Data collection: SMART (Siemens, 1996); cell refinement: SAINT (Siemens, 1996); data reduction: SAINT; program(s) used to solve structure: SHELXTL (Sheldrick, 1997); program(s) used to refine structure: SHELXTL; molecular graphics: SHELXTL; software used to prepare material for publication: SHELXTL, PARST (Nardelli, 1995) and PLATON (Spek, 2003).

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