Conformational Study of a Photochemical Cyclopentenone Rearrangement. Molecular Mechanics Calculations and *X*-Ray Structure of 14β-Hydroxy-5-methoxy-de-A-oestra-5,7,9,16-tetraen-15-one

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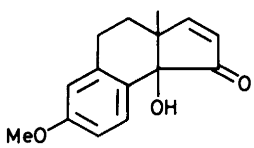
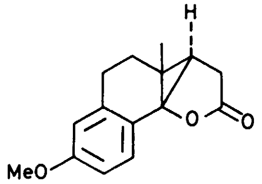
Molecular mechanics calculations show two minimum energy conformers for the title ketol (**1**), both having a ring C-sofa conformation. *X*-Ray crystal structure analysis shows that of these the 12β-sofa conformation is adopted in the ketol [$\Delta C_s(8) = 1.7°$] and ring D assumes a flattened C(14)-envelope conformation with C(14) displaced 0.315 Å below the plane of C(13), C(17), C(16), and C(15). Crystallographic data are $a = 8.591(7)$, $b = 7.969(5)$, $c = 10.089(7)$ Å, $Z = 2$, space group $P2_1$. In the preferred conformer there is significant orbital overlap between the two isolated chromophores.

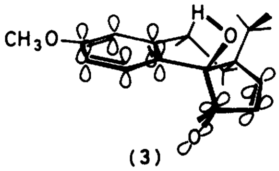
Photochemical rearrangement of the unsaturated ketol (**1**) gives the cyclopropane lactone (**2**), the structure of which has been previously established by *X*-ray analysis.[1] The rearrangement occurs readily and cleanly in diffuse sunlight, in contrast to analogous rearrangements of simpler cyclopentenones,[2,3] and in this paper we record further investigations into the factors underlying the relative ease of this reaction.



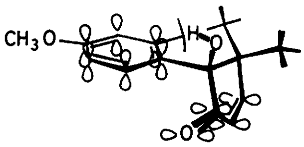
(**1**)



(**2**)



(**3**)



(**4**)

Studies of Dreiding models indicate that four possible conformations can be considered for the flexible ketol (**1**). In two of these ring C adopts a twist-boat conformation, and in the other two a sofa conformation. In all cases ring D has an envelope conformation. The twist-boat conformers are subject to some degree of torsional strain in ring C, but little torsional strain is evident in the 12α- and 12β-sofa conformers (**3**) and (**4**), both of which show near perfect staggering across bonds C(11)–C(12) and C(12)–C(13). Steric interaction between the angular methyl group at C(13) and the 14β-hydroxy group is also of similar magnitude in both of these conformers, and the main difference between them is the 1,3-diaxial interaction between the 11β-hydrogen and the 13β-methyl group in the 12α-sofa conformer (**3**). This interaction is absent in the 12β-conformer (**4**).

An *X*-ray examination of the ketol (**1**) was undertaken to provide details of the molecular conformation. The crystal structure was elucidated by direct-phasing procedures and the atomic co-ordinates adjusted by least-squares calculations. The analysis revealed the molecular structure shown in Figure 1.

The molecules are held together in the crystal by intermolecular hydrogen bonding [O(2) ··· O(3)* 2.910(9) Å, HO(2) ··· O(3)* 2.01(5) Å, O(2)–HO(2) ··· O(3)* 156(5)°]. The intramolecular distance O(2) ··· O(3) 2.903(10) Å is also short but there is no hydrogen bond here as O(3) ··· HO(2) is 2.79(6) Å and O(3) ··· HO(2) is 87(4)°.

The C/D ring junction is confirmed as *cis* with the torsion angle C(17)–C(13)–C(14)–O(2) 139.0(7)°. Ring C adopts a 12β-sofa conformation [$\Delta C_s(8) = 1.7°$] and ring D adopts a flattened envelope conformation with C(14) displaced 0.315(6) Å below the C(13)C(17)C(16)C(15) plane.

Various conformational states of the molecule were examined by molecular mechanics utilising computer program MM2.[4] Some additional parameters were included in the program, for example strain-free bond lengths of 1.395 and 1.480 Å for the aromatic and single C_{sp^2}–C_{sp^2} bonds respectively were employed.

The molecule crystallises as the 12β-conformer and force field calculations starting with this model yield a strain energy of 51.4 kJ mol^{-1}. The 12α conformer is calculated to have a strain energy of 54.1 kJ mol^{-1} indicating only a small energy difference between the two conformers. A cross section of the energy surface showing the interconversion pathway between these conformers is shown in Figure 2. The inversion path was obtained by varying the 9-11-12-13 torsion angle from its value in *each* conformer to zero. By this method the height of the inversion barrier (12β→12α) was found to be *ca.* 39 kJ mol^{-1}.

In the 12α-conformer the relative orientations of the π-electron system of the carbonyl group and the aromatic ring allow no significant orbital overlap, but in the 12β-conformer there is considerable overlap between the two chromophores. This is reflected in the C(15)–C(14)–C(8) angle being only 105° and is also reflected in the u.v. absorption at 339 nm, raising the possibility of intermediates in the photochemical rearrangement to the lactone (**2**) involving some degree of bonding between C(8) and C(15). If significant bonding does develop between these two carbon atoms, a mechanism involving the biradical intermediates (**6**)—(**8**) depicted in the Scheme could account for the results. Initial excitation could then lead to the biradical species (**6**), which could give the biradical (**7**) by homolysis of the C(14)–C(15) bond of the cyclopropane ring with regeneration of the 16-en-15-one system, followed by collapse to the precursor (**8**) of the ketene (**9**). Direct interconversion of the two cyclopropane intermediates (**6**) and (**8**) by way of the electrocyclic process depicted [arrows on formula (**6**)] is also possible. Alternatively, the C=O–π orbital interaction could merely facilitate the absorption of radiation (339 nm),

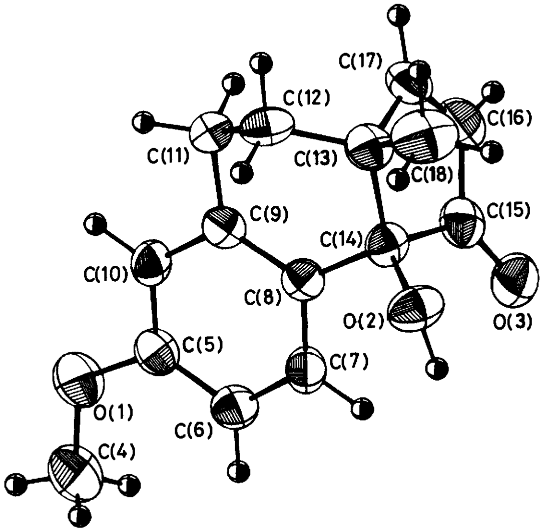


Figure 1. Atomic arrangement in ketol (**1**); thermal ellipsoids are represented at the 50% probability level

Table 1. Fractional atomic co-ordinates (× 10^4) with e.s.d.s

Atom	*x*	*y*	*z*
O(1)	8 477(7)	5 578	3 061(5)
O(2)	7 340(6)	4 125(10)	8 807(5)
O(3)	9 832(7)	6 797(11)	9 915(6)
C(4)	9 892(10)	4 675(16)	3 028(8)
C(5)	8 265(8)	5 582(13)	4 352(7)
C(6)	9 370(8)	4 841(12)	5 631(7)
C(7)	8 952(8)	4 911(12)	6 812(7)
C(8)	7 468(8)	5 688(12)	6 766(6)
C(9)	6 373(8)	6 383(11)	5 468(6)
C(10)	6 787(8)	6 350(12)	4 267(6)
C(11)	4 664(8)	7 108(12)	5 287(7)
C(12)	4 040(7)	6 271(13)	6 340(7)
C(13)	5 350(8)	6 460(13)	7 892(7)
C(14)	7 129(8)	5 709(12)	8 159(6)
C(15)	8 342(9)	7 047(12)	9 133(7)
C(16)	7 394(11)	8 594(13)	8 977(8)
C(17)	5 737(10)	8 249(12)	8 295(7)
C(18)	4 636(10)	5 657(15)	8 942(8)
HO(2)	8 442(56)	3 603(79)	9 145(63)
H(4A)	9 899(10)	4 771(16)	2 042(8)
H(4B)	9 798(10)	3 466(16)	3 253(8)
H(4C)	10 972(10)	5 152(16)	3 765(8)
H(6)	10 436(8)	4 274(12)	5 694(7)
H(7)	9 742(8)	4 385(12)	7 742(7)
H(10)	6 009(8)	6 887(12)	3 338(6)
H(11A)	4 788(8)	8 341(12)	5 485(7)
H(11B)	3 817(8)	6 912(12)	4 271(7)
H(12A)	3 843(7)	5 050(13)	6 099(7)
H(12B)	2 949(7)	6 807(13)	6 248(7)
H(16)	7 897(11)	9 727(13)	9 322(8)
H(17)	4 832(10)	9 124(12)	8 074(7)
H(18A)	4 367(10)	4 448(15)	8 686(8)
H(18B)	3 577(10)	6 260(15)	8 850(8)
H(18C)	5 507(10)	5 747(15)	9 962(8)

thereby allowing formation of an excited-state precursor of the simplest biradical (**5**), which arises by scission of the C(14)–C(15) bond.[1] However, even though the present results appear to favour reaction in the 12β-form, the Curtin–Hammett principle[5] dictates that the molecule could still react in the 12α-conformation, should this rearrange *via* a transition state of lower energy.

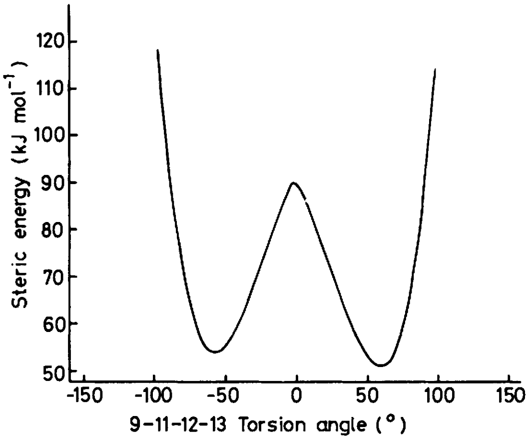


Figure 2. Interconversion between 12α- and 12β-conformer

Table 2. Bond lengths (Å) with e.s.d.s

O(1)–C(4)	1.425(11)	C(9)–C(10)	1.394(11)
O(1)–C(5)	1.386(9)	C(9)–C(11)	1.518(10)
O(2)–C(14)	1.399(12)	C(11)–C(12)	1.524(12)
O(3)–C(15)	1.218(8)	C(12)–C(13)	1.521(8)
C(5)–C(6)	1.387(9)	C(13)–C(14)	1.560(11)
C(5)–C(10)	1.381(11)	C(13)–C(17)	1.483(14)
C(6)–C(7)	1.378(11)	C(13)–C(18)	1.560(13)
C(7)–C(8)	1.401(11)	C(14)–C(15)	1.536(11)
C(8)–C(9)	1.381(8)	C(15)–C(16)	1.451(14)
C(8)–C(14)	1.547(10)	C(16)–C(17)	1.335(11)

Table 3. Bond angles (°) with e.s.d.s

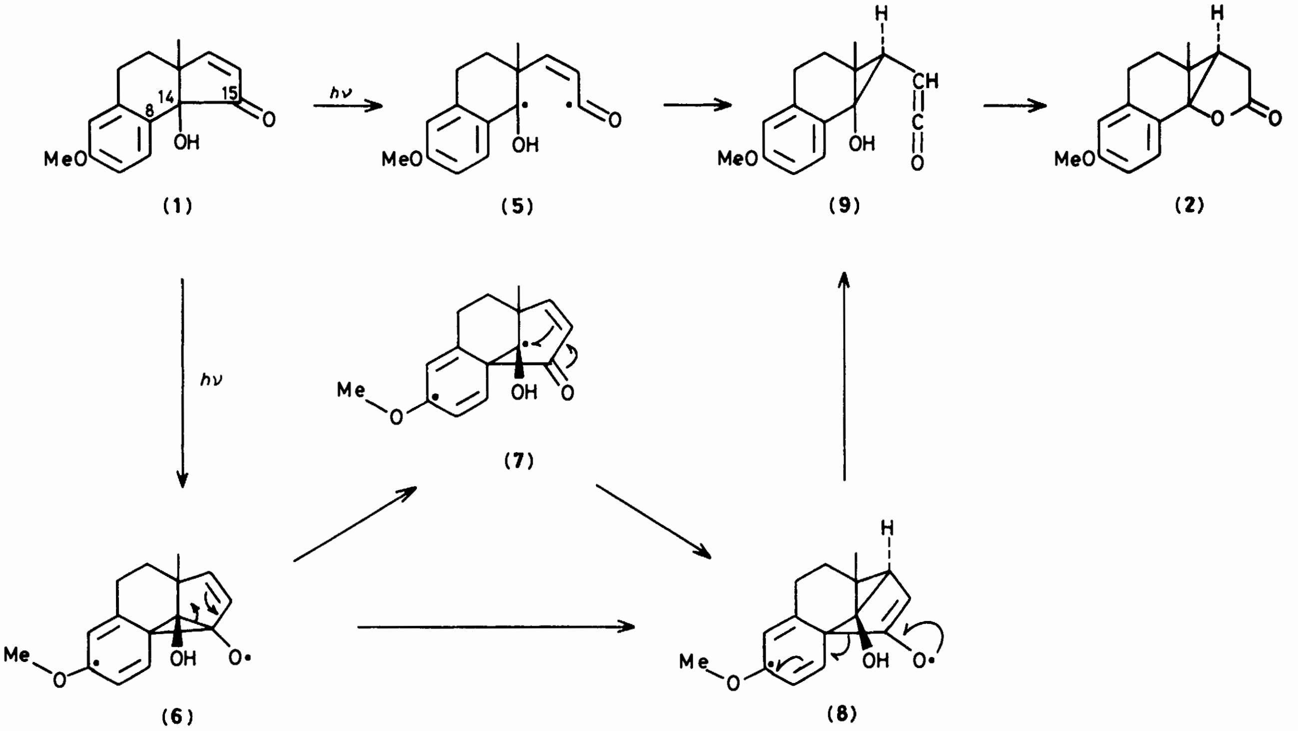
C(5)–O(1)–C(4)	117.5(5)	C(6)–C(5)–O(1)	124.9(7)
C(10)–C(5)–O(1)	114.2(6)	C(8)–C(14)–O(2)	112.2(7)
C(13)–C(14)–O(2)	111.1(6)	C(15)–C(14)–O(2)	113.7(6)
C(14)–C(15)–O(3)	124.3(9)	C(16)–C(15)–O(3)	127.3(9)
C(10)–C(5)–C(6)	120.8(6)	C(7)–C(6)–C(5)	117.9(7)
C(9)–C(10)–C(5)	120.4(6)	C(8)–C(7)–C(6)	122.8(6)
C(9)–C(8)–C(7)	118.0(6)	C(14)–C(8)–C(7)	118.6(6)
C(14)–C(8)–C(9)	123.4(7)	C(10)–C(9)–C(8)	120.0(7)
C(11)–C(9)–C(8)	121.4(6)	C(13)–C(14)–C(8)	112.3(5)
C(15)–C(14)–C(8)	105.1(6)	C(11)–C(9)–C(10)	118.5(6)
C(12)–C(11)–C(9)	110.2(6)	C(13)–C(12)–C(11)	110.6(6)
C(14)–C(13)–C(12)	113.9(6)	C(17)–C(13)–C(12)	111.6(7)
C(18)–C(13)–C(12)	109.1(7)	C(17)–C(13)–C(14)	103.1(7)
C(18)–C(13)–C(14)	110.6(7)	C(15)–C(14)–C(13)	102.0(7)
C(18)–C(13)–C(17)	108.3(7)	C(16)–C(17)–C(13)	114.4(8)
C(16)–C(15)–C(14)	108.4(7)	C(17)–C(16)–C(15)	108.4(9)

Experimental

Crystal Data.—$C_{15}H_{16}O_3$, $M = 244.3$. Monoclinic, $a = 8.591(7)$, $b = 7.969(5)$, $c = 10.089(7)$, $\beta = 113.90(6)°$. $U = 631.5$ Å^3, $Z = 2$, $D_c = 1.28$ g cm^{-3}, $F(000) = 260$, Mo-K_α radiation, $\lambda = 0.710$ Å, $\mu = 0.51$ cm^{-1}. Space group $P2_1$.

Crystallographic Measurements.—Intensity measurements were obtained from a Nicolet P3 automated diffractometer. Integrated relative intensities for 1 110 independent reflections with $2\theta < 50°$ were measured as θ—2θ scans; 863 reflections had $I > 2.5\sigma(I)$.

Structure Analysis.—The crystal structure was elucidated by direct methods using the MULTAN program.[6] Hydrogen atoms were observed in electron density maps calculated at intermediate stages of structure refinement.[7] The co-ordinates



Scheme.

Table 4. Torsion angles (°) with e.s.d.s

C(4)–O(1)–C(5)–C(6)	3.2(11)	C(4)–O(1)–C(5)–C(10)	−174.4(7)
O(1)–C(5)–C(6)–C(7)	−178.1(7)	C(10)–C(5)–C(6)–C(7)	−0.6(12)
O(1)–C(5)–C(10)–C(9)	177.3(7)	C(6)–C(5)–C(10)–C(9)	−0.5(12)
C(5)–C(6)–C(7)–C(8)	0.2(12)	C(6)–C(7)–C(8)–C(9)	1.2(12)
C(6)–C(7)–C(8)–C(14)	−179.5(7)	C(7)–C(8)–C(9)–C(10)	−2.2(11)
C(7)–C(8)–C(9)–C(11)	174.4(7)	C(14)–C(8)–C(9)–C(10)	178.5(7)
C(14)–C(8)–C(9)–C(11)	−4.9(11)	C(7)–C(8)–C(14)–O(2)	−48.4(9)
C(7)–C(8)–C(14)–C(13)	−174.4(7)	C(7)–C(8)–C(14)–C(15)	75.6(8)
C(9)–C(8)–C(14)–O(2)	130.9(8)	C(9)–C(8)–C(14)–C(13)	4.9(10)
C(9)–C(8)–C(14)–C(15)	−105.1(8)	C(8)–C(9)–C(10)–C(5)	1.9(12)
C(11)–C(9)–C(10)–C(5)	−174.8(7)	C(8)–C(9)–C(11)–C(12)	−26.1(10)
C(10)–C(9)–C(11)–C(12)	150.6(7)	C(9)–C(11)–C(12)–C(13)	56.6(8)
C(11)–C(12)–C(13)–C(14)	−58.2(9)	C(11)–C(12)–C(13)–C(17)	57.9(9)
C(11)–C(12)–C(13)–C(18)	177.6(7)	C(12)–C(13)–C(14)–O(2)	−100.0(8)
C(12)–C(13)–C(14)–C(8)	26.6(9)	C(12)–C(13)–C(14)–C(15)	138.6(7)
C(17)–C(13)–C(14)–O(2)	139.0(7)	C(17)–C(13)–C(14)–C(8)	−94.4(7)
C(17)–C(13)–C(14)–C(15)	17.5(8)	C(18)–C(13)–C(14)–O(2)	23.4(9)
C(18)–C(13)–C(14)–C(8)	149.9(7)	C(18)–C(13)–C(14)–C(15)	−98.1(7)
C(12)–C(13)–C(17)–C(16)	−134.1(8)	C(14)–C(13)–C(17)–C(16)	−11.5(10)
C(18)–C(13)–C(17)–C(16)	105.8(9)	O(2)–C(14)–C(15)–O(3)	40.0(11)
O(2)–C(14)–C(15)–C(16)	−138.6(7)	C(8)–C(14)–C(15)–O(3)	−83.1(10)
C(8)–C(14)–C(15)–C(16)	98.3(8)	C(13)–C(14)–C(15)–O(3)	159.6(8)
C(13)–C(14)–C(15)–C(16)	−19.0(8)	O(3)–C(15)–C(16)–C(17)	−165.5(9)
C(14)–C(15)–C(16)–C(17)	13.0(10)	C(15)–C(16)–C(17)–C(13)	−0.6(11)

and anisotropic thermal parameters for the non-hydrogen atoms were varied in least-squares calculations. The C–H distances were constrained to be equal to 1.00 Å and these hydrogen atoms were allowed to ride on their directly bonded carbon atoms during refinement. The hydroxy hydrogen was not constrained and the final O–H distance was 0.96(5) Å. Unit weights were employed and refinement converged at *R* 5.5%.

Final positional parameters are listed in Table 1, bond lengths in Table 2, bond angles in Table 3, and torsion angles in Table 4. Thermal parameters are listed in Supplementary Publication No. SUP 56094 (3 pp.).*

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Received 30*th March* 1984; *Paper* 4/521