

A NOVEL ACID CATALYSED CYCLIZATION - SYNTHESIS AND X-RAY CRYSTAL STRUCTURE  
ANALYSIS OF 8-ACETOXY-6-(2,4-DIMETHOXY-5-BROMOPHENYL)-3-METHYLTRICYCLO(5,2,1,0<sup>3,8</sup>)DECAN-2-ONE

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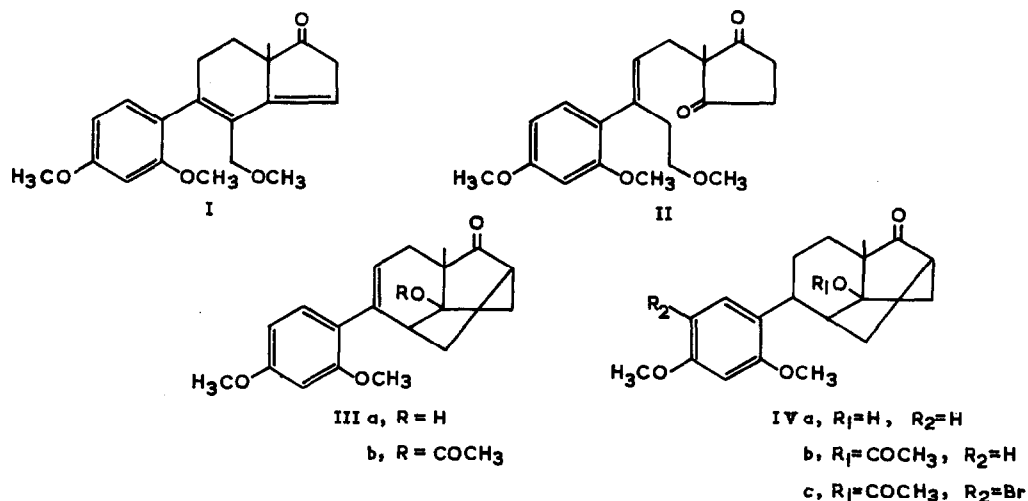
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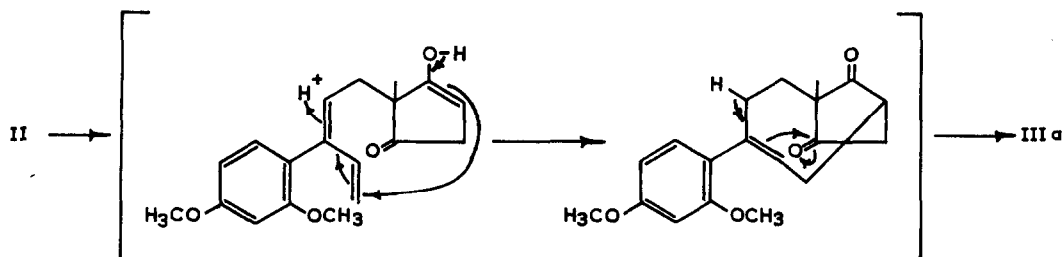
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In connection with the total synthesis of heterocyclic steroids, we undertook the synthesis of a B-secosteroid intermediate (I) starting from 2',3,4'-trimethoxypropiophenone [1]. Examples involving a 'B-seco' approach for the total synthesis of steroids are the synthesis of oestrone [2] and steroids without ring B [3]. We wish to report in this communication the structure of a novel steroid derivative without ring B by an acid catalysed bis cyclization. Incidentally, this forms a new approach to the synthesis of homobrendane derivatives [4].

Grignard reaction of 2',3,4'-trimethoxypropiophenone with vinyl magnesium bromide followed by condensation with 2-methylcyclopentane-1,3-dione afforded the diketone (II) [5] ( $M^+$  346), NMR ( $CDCl_3$ ): 1.17 (3H,  $CH_3$ ), 3.22 (3H, OMe), 3.75, 3.81 (6H, aromatic OMe) and 5.24  $\delta$  [1H, t (J=9 Hz)]. Refluxing a solution of II in 20% ethanolic HCl for 1 hr resulted in a mixture of products from which a crystalline solid (IIIa), m.p. 125-6°, could be obtained (20%). This solid (IIIa) ( $M^+$  314) showed the presence of OH and C=O groups (IR) and exhibited peaks in the NMR at 1.13 (3H, Me), 1.7-2.2 (m, 9H), 3.79 (6H, aromatic OMe), 5.52 [1H, t (J=7 Hz)], 6.3-6.5 (m, 2H) and 6.98  $\delta$  [1H, d (J=9 Hz)]. Acetylation gave the acetate (IIIb) ( $M^+$  356), m.p. 143-4°, which on hydrolysis gave back the original alcohol (IIIa). A sharp singlet at 4.94  $\delta$  in the NMR spectrum of IIIa in  $DMSO-d_6$  indicated the tertiary nature of the



hydroxyl group [6]. Catalytic hydrogenation of IIIa (Pd/C in EtOH) yielded a dihydro compound (IVa) ( $M^+$  316), m.p. 160-1°. The aforementioned data can be explained on the basis of a 6-(2,4-dimethoxyphenyl)-2-keto-3-methyltricyclo (5,2,1,0<sup>3,8</sup>)dec-5-ene-8-ol (IIIa) structure for this alcohol. The formation of this alcohol can be visualized as follows:



Similar acid catalysed enol-ene additions are documented in literature [7]. It is not clear at present whether this goes by a concerted or a stepwise mechanism.

Single crystal X-ray analysis of the bromo derivative of IIIa confirmed this structure unambiguously. Treatment of the acetate of the dihydro alcohol (IVb), m.p. 169-70° ( $M^+$  358) with dioxane dibromide in ether [8] gave the bromo compound (IVc), m.p. 202-3° ( $M^+$  436 Br<sup>79</sup>), NMR(CDCl<sub>3</sub>): 6.42(s, 1H), 7.08 (s, 1H) and 7.24 δ (s, 3H, 0.5M benzene of crystallization). Transparent crystals of IVc were grown by slow evaporation from a solution containing benzene and petroleum ether. The unit cell dimensions and the space group of the crystal as determined from conventional

oscillation and Weissenberg photographs are as follows:  $a = 11.68 \pm 0.02 \text{ \AA}$ ,  $b = 12.91 \pm 0.02$ ,  $c = 10.43 \pm 0.02$ ;  $\alpha = 114.7 \pm 1^\circ$ ,  $\beta = 90.2 \pm 1^\circ$ ,  $\gamma = 118.25 \pm 1^\circ$ . Space group:  $P1$  or  $P\bar{1}$  ( $P\bar{1}$  confirmed from structure analysis). The density measured by flotation in aqueous potassium iodide solution indicated the presence of two molecules of IVa and one molecule of benzene in the unit cell. Intensity data were collected from the reciprocal levels  $hko$  and  $Hkl$ ,  $H=0$  to 7 from specimens cut along the crystallographic  $c$ - and  $a$ -axes respectively. The intensities were estimated visually by comparison with a calibrated standard strip and were corrected for Lorentz and polarisation factors, spot shape and absorption effects.

The structure was solved by the heavy atom method. The position of the bromine atom was determined from the  $okl$  and  $hko$  Patterson maps. The subsequent Fourier maps did not, however, reveal the entire structure due to large overlap of atomic positions. A three-dimensional Patterson map was next computed and the position of the bromine atom was confirmed. The 3D bromine-phased Fourier map had a large number of extra peaks. However, the rest of the atoms could be located by checking with the Patterson map and by trial calculations. The positional and thermal parameters of the atoms were refined by block-diagonal least-squares method to an R value of 8.6% for 2033 observed reflections. A difference electron density map was computed after completing the refinement procedure and the positions of all the hydrogen atoms were determined. The coordinates of the hydrogen atoms were not, however, refined. Superimposed sections of the final electron density map drawn perpendicular to the  $a$ -axis is shown in Fig.1. The six-membered ring in the 'cage' part of the molecule exists in a chair form and both the 5-membered rings assume envelope conformations. In this system some of the bond lengths and bond angles differ considerably from the normal values. This feature is observed in many other strained molecules [9] also. A detailed discussion of the molecular geometry and packing in the crystal will be given elsewhere.

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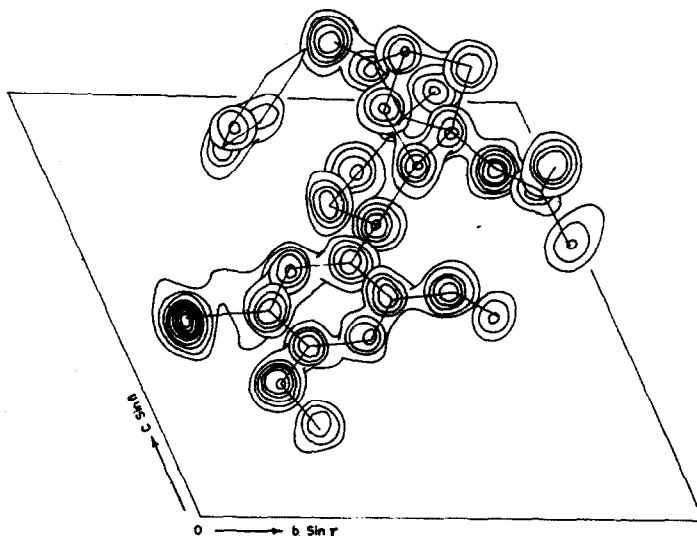


Fig.1. Superimposed sections of the final electron density map

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