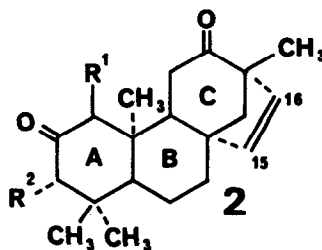
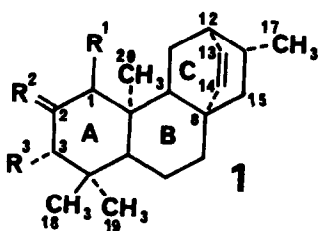


THE X-RAY CRYSTAL AND MOLECULAR STRUCTURE OF
ent-1 α -p-BROMOBENZOYLOXY-16S-ATIS-13-EN-2-ONE

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(Received in UK 7 May 1973; accepted for publication 18 May 1973)

The marked unreactivity of the ent-16S-atis-13-en system¹ as in compounds (1a-e) and the unusual² acetoxylation at C(1) on acetolysis of an ent-3 β -tosyloxybeyer-2-ketone system derived from compound (2a), was reported recently. The n.m.r. spectrum of the solvolysis product (2b) of the tosylate of (2a) (broad singlet, W_x 3 Hz at τ 5.8 due to the H(1 α) equatorial proton) suggested that long range ("W rule") coupling takes place between the H(1 α) and the H(3 α) equatorial protons via the C(2) carbonyl carbon.³



1	R ¹	α	R ²	β	R ³	2	R ¹	R ²
a	p.BrC ₆ H ₄ CO ₂	O	O	H	H	a	H	OH
b	H	OH	H	OH	OH	b	OAc	H
c	H	O	O	OH	OH			
d	OAc	O	O	H	H			
e	OH	O	O	H	H			

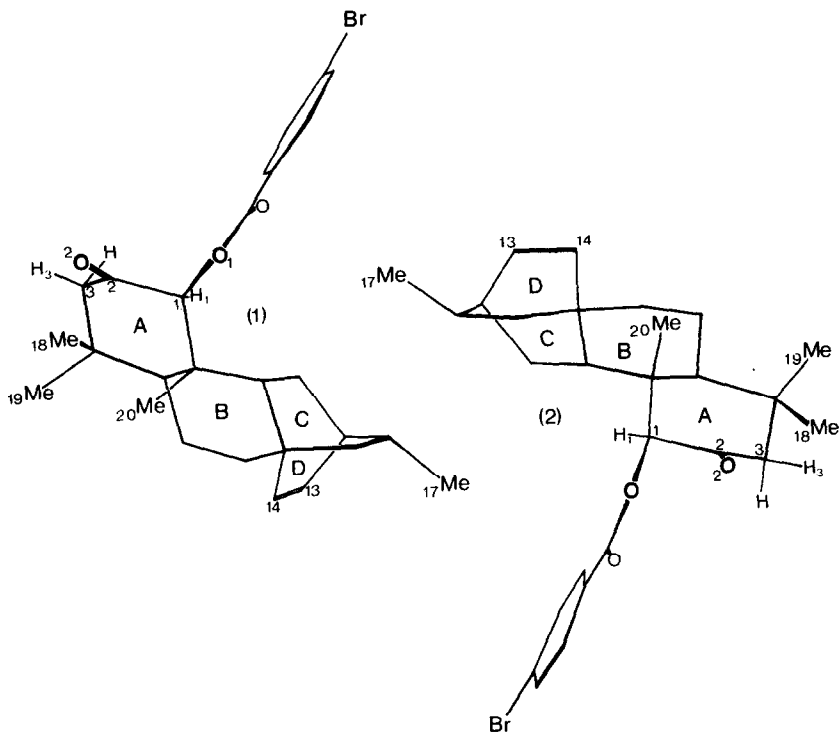
These features prompted us to undertake an x-ray structural investigation in order to obtain a detailed picture of the

stereochemical interactions involved and in particular, to determine the structure of the product of the ring A rearrangement. We decided to combine the two problems in one molecule suitable for such a structural investigation and ent-16S-1 α -p-bromobenzoyloxy-13-en-2-one (1a) was therefore prepared as described below.

Sodium borohydride reduction of the tosylhydrazone of the beyerane ketol (2a) gave ent-2 β ,3 β -dihydroxy-16S-atis-13-ene (1b). The vicinal diol function in (1b) was oxidised within a few minutes at 80° with silver carbonate on celite in benzene to the original 3 α -hydroxy-2-ketone system to give compound (1c). Acetolysis of the tosylate of (1c) gave ent-1 α -acetoxy-16S-atis-13-en-2-one (1d), τ 5.63 (1H, broad s, $W_{\frac{1}{2}}$ 3H₂, H-1 α). A methanol solution of the acetate (1d) on treatment with a few drops of dilute sodium hydroxide at room temperature rapidly deposited crystals of the corresponding alcohol (1e) which reluctantly reacted with p-bromobenzoyl chloride in pyridine to give the p-bromobenzoate (1a), m.p. 166-170°, τ 5.40 (1H, s, $W_{\frac{1}{2}}$ 3 Hz, H-1 α).

Suitable crystals of (1a), C₂₇H₃₃BrO₃, obtained from a mixture of acetone, ethanol and hexane, were triclinic, space group P1, $a=7.34$, $b=12.47$, $c=14.38$ ($\pm 0.01\text{\AA}$), $\alpha=109.3$, $\beta=97.6$, $\gamma=92.3$ ($\pm 0.01^\circ$), $U=1227\text{\AA}^3$, $D_m=1.32\text{ gcm}^{-3}$, $Z=2$; no required molecular symmetry. Intensity data were collected on a Philips four-circle diffractometer with Zr-filtered Mo-K α radiation. The structure was solved by the heavy atom and Fourier methods, and refined isotropically (Br atoms anisotropic) by block diagonal least-squares to $R = 0.09$ for 2170 observed data. Further refinement⁴ is continuing.

The two independent molecules in the asymmetric unit are related by a pseudo two fold axis, and are essentially identical (Figure: a projection down a). All bond lengths and angles are normal: Br-C(ph) 1.86 \AA , C(13)-C(14) 1.33 \AA . The results confirm that the rearrangement of the C/D ring system has taken place as proposed. The four atoms of the double bond system, C(12)-C(13)-C(14)-C(8), are coplanar within 0.01 \AA . The extreme inertness of the C(13)-C(14) double bond is clearly caused by the close contacts between it and methyl carbons C(17) and C(20), which must hinder the approach of incoming reactants: C(17)···C(13) = 3.10 \AA , C(20)···C(14) = 3.17 \AA . In addition, C(20) is further buttressed by methyl carbon C(19); C(20)···C(19) = 3.21 \AA .



Several aspects of the H^1 n.m.r. spectrum can now be explained. The short methyl $C(17)\cdots C(14)$, and methyl $C(20)\cdots C(13)$ separations place these methyl protons in the shielding environment of the $C(13)-C(14)$ double bond π cloud and as a consequence of this, their resonances appear at τ 9.33 and 9.30 respectively. The atoms $H(1)-C(1)-C(2)-O(2)-C(3)-H(3)$ are coplanar within 0.05 Å. The hydrogen atoms $H(1)$ and $H(3)$ are thus part of a W system which is the cause of the broadening of the NMR signal of $H(1)$.³

The torsion angle, methyl $C(20)-C(10)-C(1)-O(1)$, is 177° ; $C(20)$ and $O(1)$ are almost ideally trans diaxial. The torsion angle $O(1)-C(1)-C(2)-O(2)$ is large, 130° . The low reactivity of the ketol system in (1e) towards T.T.C. reagent is probably caused by the steric hindrance of the equatorial hydrogen atom at $C(1)$ by the hydrogen atoms at $C(11)$. That the solvolysis of the A ring 3α -tosyloxy-2-ketone function, should have yielded the axial product, the 1β -acetoxy-2-ketone function, implies that the approach to $C(1)$ from the α -side of the molecule in the final transition state is considerably hindered, because a regular S_N2' reaction would produce the equatorial isomer.⁵ This hindrance is caused by the methyl group $C(20)$.

We thank Dr. Gert Kruger, National Physical Research Laboratory, C.S.I.R., Pretoria, who collected the intensity data, and Dr. E.S. Waight, Chemistry Department, Imperial College, London, for the accurate mass determinations. This work was supported by grants from the South African Council for Scientific and Industrial Research.

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