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Boat Forms of Ring A in B-Norsteroids

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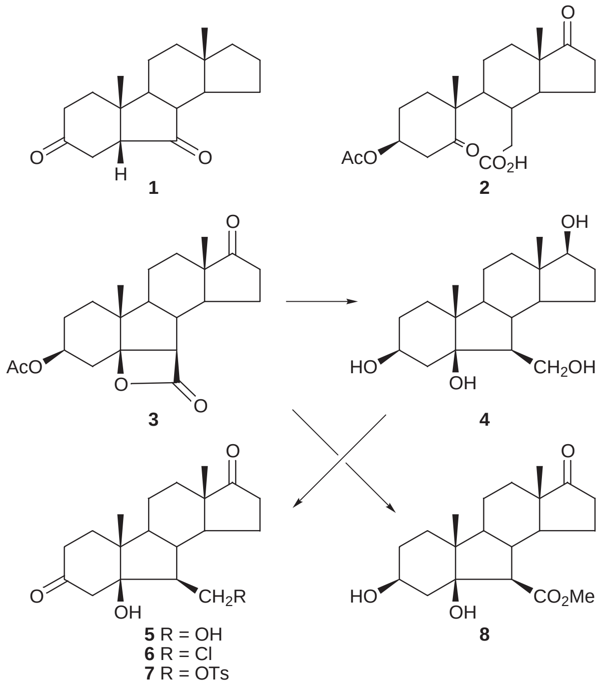
The X-ray crystal structures of 6β-toluene-*p*-sulfonyloxymethyl-5β-hydroxy-B-norandrostane-3,17-dione (**7**) and 6β-methoxycarbonyl-3β,5β-dihydroxy-B-norandrostan-17-one (**8**) reveal that ring A exists in a twisted boat form in these 5β-B-norandrostanes.

In the course of studies on the relative stability of the *cis* and *trans* A/B fusion of B-norsteroids, we examined the X-ray crystal structure of B-nor-5β-androstane-3,6-dione **1**.[1] This showed that ring A of this compound was in the boat form whilst the corresponding B-nor-5α-androstane possessed ring A in the chair form. Although the distortion of ring A away from a pure chair form is quite common,[2,3] particularly for 4,4-dimethyl-3-ketones,[4] the existence of boat forms is more unusual.[5–8] Here, we report the crystal structure of two further examples of B-nor-5β-androstanes in which ring A exists in a boat form.



1 **2** **3** **4**

5 R = OH
6 R = Cl
7 R = OTs

8

B-Norsteroids are formed by the cyclization of 5-oxo-5,6-secoandrostan-6-oic acids to give β-lactones as exemplified by the conversion of **2** to **3**.[9] Pyrolysis of these β-lactones leads to the loss of carbon dioxide and the formation of the B-norandrost-5-ene. However reduction of **3** with lithium aluminium hydride gave the tetra-ol **4**. Selective oxidation of the tetra-ol with *N*-bromosuccinimide[10] gave the 3,17-diketone **5**. This compound gave a mono-acetate on treatment with acetic anhydride in pyridine. Attempts to prepare the 5β,7-oxetane by treatment with toluene-*p*-sulfonyl chloride were unsuccessful and gave instead the 7-chloride **6** and the 7-toluene-*p*-sulfonate **7**. More vigorous conditions led to decomposition whilst prolonged treatment with toluene-*p*-sulfonyl chloride led to the conversion of the toluene-*p*-sulfonate to the chloride **6**.

Hydrolysis of the β-lactone **3** with methanolic potassium carbonate or with a catalytic amount of tetracyanoethylene in methanol gave the hydroxy-ester **8**.

Since the β-lactone **3** is formed relatively easily, the reluctance to form a 5β, 7-oxetane seemed surprising and we therefore examined the X-ray crystal structure of the 7-toluene-p-sulfonate **7** in case epimerization had taken place, for example at C-6, during the reduction of the lactone. The X-ray crystal structure (Fig. 1) confirmed that the *cis* A/B ring junction and the stereochemistry at C-6 had been retained but it also showed that ring A existed in a twisted boat form in this steroid. The endocyclic torsion angles for ring A are given in Table 1. This geometry has the effect of moving the 5β-hydroxy group away from the C-6 substituent and thus diminishes the possibility of oxetane formation. We then considered the possibility that the existence of ring A in a boat form required the presence of both the *cis* A/B fusion and a 3-ketone. However the

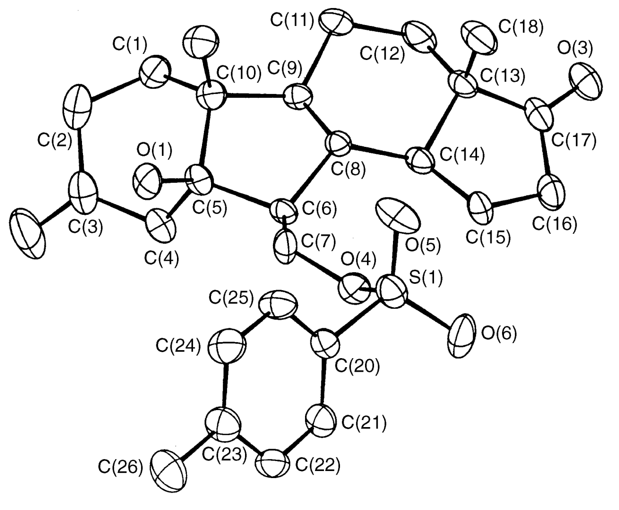


Fig. 1 X-Ray crystal structure of compound **7**

Table 1 Endocyclic torsion angles (°) for ring A

	Compound		
Bond	**1**	**7**	**8**
C(10) C-1 C-2 C(3)	−54.8	−57.9	−66.6
C(1) C-2 C-3 C(4)	6.2	17.5	24.6
C(2) C-3 C-4 C(5)	47.1	40.4	38.1
C(3) C-4 C-5 C(10)	−54.3	−61.0	−63.7
C(4) C-5 C-10 C(1)	7.8	22.0	21.6
C(5) C-10 C-1 C(2)	46.3	36.9	39.9

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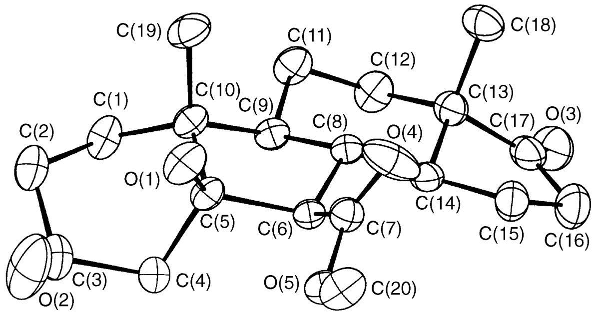

Fig. 2 X-Ray crystal structure of compound **8**

X-ray crystal structure of the hydroxy-ester **8** (Fig. 2) showed that ring A existed in a twisted boat form in this compound as well.

A possible explanation for the existence of ring A in these twisted boat forms is that when there is a *cis* A/B ring junction and a five membered ring B these conformations minimize the interactions between C-1 and C-11 and between C-4 and the C-6 substituent.

Experimental

Crystal Data and Structure Determinations.—(*a*) Compound **7**: $C_{26}H_{36}O_{6}5$, $M_r = 474.6$, orthorhombic, space groups $P2_12_12_1$ (no. 19), $a = 6.056(2)$, $b = 20.926(3)$, $c = 9.835(2)$ Å, $\beta = 105.79(2)^\circ$, $V = 1199.3(5)$ Å^3, $Z = 2$, $D_c = 1.31$ g cm^{-3}, $F(000) = 508$, $\lambda = 1.5418$ Å, $\mu = 1.53$ mm^{-1}. Data were collected using a crystal of size 0.2 × 0.2 × 0.2 mm on an Enraf-Nonius CAD4 diffractometer. A total of 1401 reflections were collected for $2 < \theta < 50^\circ$ and $0 < h < 6$, $0 < k < 20$, $-0 < l < 9$. There were 1264 unique reflections and 1228 reflections with $I > 2\sigma(I)$ were used in the refinement.

(*b*) Compound **8**: $C_{20}H_{30}O_5$, $M_r = 350.4$, monoclinic, space groups $P2_1$ (no. 4), $a = 5.911(8)$, $b = 13.630(3)$, $c = 11.759(2)$ Å, $\beta = 99.037(14)^\circ$, $V = 948.3(3)$ Å^3, $Z = 2$, $D_c = 1.23$ g m^{-3}, $F(000) = 380$, $\lambda = 0.71073$ Å, $\mu = 0.09$ mm^{-1}. Data were collected using a crystal of size 0.2 × 0.2 × 0.1 mm on an Enraf-Nonius CAD4 diffractometer. A total of 1897 reflections were collected for $2 < \theta < 25^\circ$ and $0 < h < 7$, $0 < k < 16$, $-13 < l < 13$. There were 1736 unique reflections and 1333 reflections with $I > 2\sigma(I)$ were used in the refinement.

The structures were solved by direct methods using SHELXS-97[11] (SHELXS-86 for compound **7**) and SHELXL-97 (SHELXL-93 for compound **7**)[12] for the refinement. The non-hydrogen atoms were refined anisotropically by full-matrix least squares on F^2. Hydrogen atoms were included in the riding mode with $U_{\rm iso}(\rm H) = 1.2U_{\rm eq}(\rm C)$ or $1.5_{\rm eq}(\rm C)$ for methyl groups. The hydroxyl group was riding at an idealised geometry with $U_{\rm iso}(\rm H) - 1.5U_{\rm eq}(\rm O)$. The final R indices for compound **7** were $R_1 = 0.044$, $wR_2 = 0.109$ and R indices (all data) $R_1 = 0.045$, $wR_2 = 0.111$. The goodness-of-fit on F^2 was 1.082 and the maximum shift/esd was 0.009. The final R indices for compound **8** were $R_1 = 0.043$, $wR_2 = 0.093$ and R indices (all data) $R_1 = 0.064$, $wR_2 = 0.102$. The goodness-of-fit on F^2 was 1.049 and the maximum shift/esd, was 0.001. Tables of atomic coordinates, bond lengths and angles, anisotropic displacement factors and hydrogen atom coordinates are given in the appendix (see full text).

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Techniques used: ^{1}H NMR, IR, X-ray crystallography

References: 12

Appendix: Crystallographic data for compounds **7** and **8**

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