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A ^{13}C NMR Method for Determining the Stereochemistry of the A/B Ring Junction in B-Norsteroids

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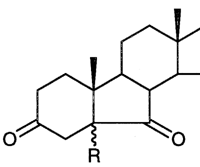
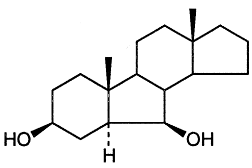
A correlation between the position of the ^{13}C NMR signal for the C-10 methyl group (C-19) and the stereochemistry of the A/B ring junction has been established and applied to the determination of the stereochemistry of the products of the hydroboration of B-norandrosta-3,5-dien-17-one.

In general when rings A and B of a steroid are six-membered the *trans* A/B ring junction is more stable than the *cis* ring junction. However when either ring A or ring B is five-membered, the *cis* ring junction can be favoured.[1] Although the stereochemistry of individual compounds in the B-nor series has been established by optical rotatory dispersion studies and by ^{1}H NMR methods,[2,3] there is a need for a spectroscopic correlation which reflects the stereochemistry of the A/B ring junction. In the normal six-membered steroid series there is a significant difference in the chemical shift of the ^{13}C NMR signals for the C-10 methyl group (C-19) between the 5α- and 5β-androstane series (δ_C 12.3 for 5α-androstane; δ_C 24.3 for 5β-androstane).[4] Examination of the ^{13}C NMR spectra for a series of B-norsteroids reveals that a similar correlation exists in the B-norsteroids. In the B-nor-5α-androstanes the resonance lies in the region δ 13–15 whilst in the B-nor-5β-androstanes the signal lies in the region δ 22–25.



9 R = α-H
10 R = β-H



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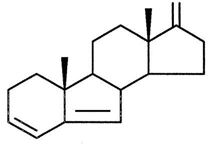
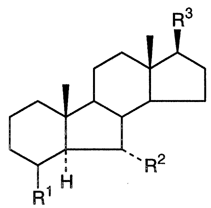
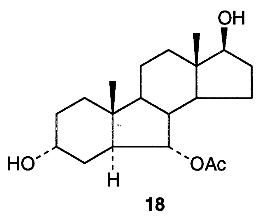


14



15 R^1 = α-OAc, R^2 = α-OH, R^3 = OAc
16 R^1 = β-OH, R^2 = α-OAc, R^3 = OAc
17 R^1 = H, R^2 = α-OAc, R^3 = OH



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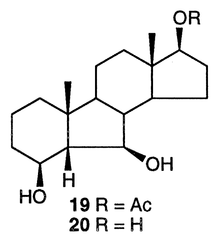

19 R = Ac
20 R = H

In the course of establishing the stereochemistry of the model compounds for this work, B-nor-5α-androstane-3,6-dione **9** was treated with methanolic potassium hydroxide to give B-nor-5β-androstane-3,6-dione **10**. An X-ray crystal structure of **10** (Fig. 1) showed that isomerization had only taken place at C-5 and not at C-8. Reduction of the diketone **9** with sodium borohydride gave the 3β,6β-diol **7**. Because of the facility with which isomerization took place at C-5, the stereochemistry of this compound was also established by X-ray crystallography (Fig. 2).

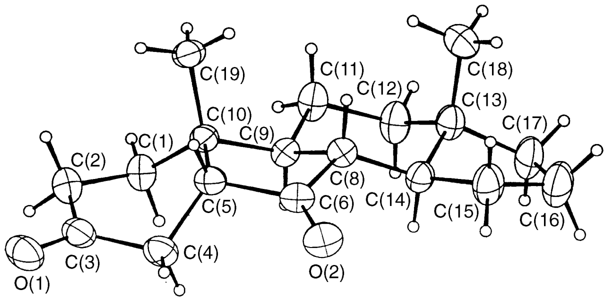

Fig. 1 X-Ray crystal structure of compound **10**

The ^{13}C NMR correlation was then applied to establishing the stereochemistry of the products of hydroboration of B-norandrosta-3,5-dien-17-one **14**. This gave a complex mixture of products (Table) which were separated only after acetylation and in some instances further hydrolysis with methanolic potassium hydroxide. The distribution of products was similar to that obtained from androsta-3,5-dien-17-one but with a slightly higher proportion of α-face attack.[11]

Experimental

Crystallographic Data and Structure Determination.—Compound **7**, $C_{18}H_{30}O_2 \cdot H_2O$, M_r 296.4, orthorhombic, space group $P2_12_12_1$ (no. 19), $a = 6.522(2)$, $b = 9.511(5)$, $c = 28.428(6)$ Å, $V = 1763(1)$ Å^3, $T = 293$ K, $Z = 4$, $D_c = 1.12$ g cm^{-3}, $F(000) = 656$, monochromated Mo-Kα radiation, $\lambda = 0.71073$ Å, $\mu = 0.07$ mm^{-1}. Data were collected using a crystal of size $0.30 \times 0.30 \times 0.15$ mm on an Enraf-Nonius CAD4 diffractometer. A total of 1821 reflections were collected for $2 < \theta < 25°$ and $0 < h < 7$, $0 < k < 11$ and $0 < l < 33$.

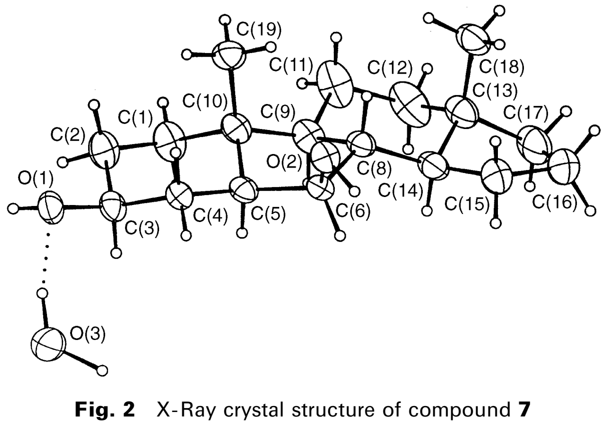

Fig. 2 X-Ray crystal structure of compound **7**

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Table Products of Hydroboration of B-norandrosta-3,5-dien-17-one **14**

	% Yield	C-19
B-nor-5α-androstanes		
15	7.8	13.1
16	3.0	13.0
17	5.6	13.7
18	6.8	11.6
B-nor-5β-androstanes		
19	2.1	24.8
20	9.4	26.0

1168 Reflections with $I > 2\sigma(I)$ were used in the refinement. There was no crystal decay and no absorption correction was applied.

The structure was solved by direct methods using SHELXS-86[15] and SHELXL-93.[16] The non-hydrogen atoms were refined anisotropically by full matrix least squares. Hydrogen atoms were included in riding mode with $U_{iso} = 1.2U_{eq}(C)$ or $1.5U_{eq}(C)$ for methyl groups. The final R indices were $R_1 = 0.048$ and $wR_2 = 0.125$ and R indices (all data): $R_1 = 0.108$, $wR_2 = 0.161$. The maximum shift/e.s.d. was 0.002.

Compound **10**, $C_{18}H_{26}O_2$, M_r 274.4, orthorhombic, space group $P2_12_12_1$ (no. 19), $a = 6.283(2)$, $b = 10.608(5)$, $c = 23.714(6)$ Å, $V = 1581(1)$ Å^3, $T = 293$ K, $Z = 4$, $D_c = 1.15$ g cm^{-3}, $F(000) = 600$, monochromated Mo-Kα radiation, $\lambda = 0.71073$ Å, $\mu = 0.07$ mm^{-1}. Data were collected using a crystal of size $0.30 \times 0.20 \times 0.20$ mm on an Enraf-Nonius CAD4 diffractometer. A total of 1881 reflections were collected for $2 < \theta < 26°$ and $0 < h < 7$, $0 < k < 13$ and $0 < l < 29$. 1669 Reflections with $I > 2\sigma(I)$ were used in the refinement. There was no crystal decay and no absorption correction was applied.

The structure was solved as above. The final R indices were $R_1 = 0.035$ and $wR_2 = 0.101$ and R indices (all data): $R_1 = 0.042$, $wR_2 = 0.107$. The maximum shift/e.s.d. was 0.001.

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

Tables: 4

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Appendix: Tables of crystallographic data for **7** and **10**

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