ANDROSTA-4,16-DIENE-3,6-DIONE: AN UNKNOWN MEMBER AMONG THE SMELLING ANDROST-16-ENES

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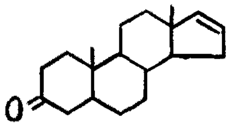
ABSTRACT

The synthesis of a still-unknown member of the physiologically interesting 16-unsaturated C_{19} steroids - androsta-4,16-diene-3,6-dione - is described. The spectroscopic data of the new compound are reported.

INTRODUCTION

In a new procedure for preparing 5α-androst-16-en-3-one 1 in tritium-labeled form (1), the well-known gentle Jones oxidation (2) was used to oxidize the remaining unconverted androsta-5,16-dien-3β-ol 2 to androsta-5,16-dien-3-one 3 . Unexpectedly, a uv-active product with a markedly smaller R_f value than that of the ketone 1 was found. This product was to be synthesized and characterized.



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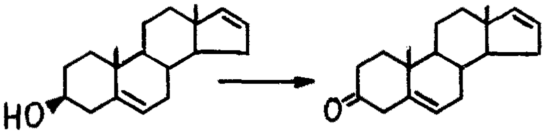

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EXPERIMENTAL

Materials and methods: Jones reagent (26.72 g CrO_3 + 23 mL H_2SO_4(conc.) + H_2O to 100 mL) was used to oxidize the dienol 2 (3). The conversion of the dienol and the purity of the chromatographically purified oxidation product were controlled by thin-layer chromatography (TLC) on analytic silufol plates (Kavalier, CSSR), using benzene/acetone (9 : 1) as solvent. After spraying with vanillin in sulfuric acid and heating, all the spots on the silufol plates were visible. The column chromatography for purifying the oxidation product was carried out with silica gel for TLC (Merck, FRG) in a column (420 mm x 25 mm), which was also eluted by benzene/acetone (9 : 1).

The following devices were used for measuring the spectroscopic data: UV, DK-2A (Beckman,USA); IR, U 20 (Carl Zeiss,GDR); MS, JMS D 100 (Japan); ^{13}C-NMR, WH 90 DS (22.635 MHz, Bruker-Spectrospin).

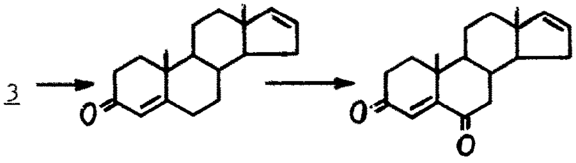
Jones oxidation of androsta-5,16-dien-3ß-ol 2 : The dienol 2 (960 mg = 3.5 mmol) was dissolved in acetone (125 mL) and cooled to 0°C. Under stirring, Jones reagent (2.5 mL) was added dropwise, after which a visible yellow color persisted. Excess reagent was reduced with isopropanol after 1 h . The reaction mixture was poured into water (250 mL) and extracted with benzene (2 x 50 mL). The organic extract was washed with water, dried (Na_2SO_4), and then the benzene was removed *in vacuo*. The oily residue was purified by column chromatography. White product (854 mg), mp 130°C (ethanol).

RESULTS AND DISCUSSION

As can be seen from the spectroscopic data, the oxidation product of the dienol 2 has a 3-keto-Δ^4-6-keto structure. Therefore, there is no doubt that the Jones oxidation does not stop at the dienone 3 but passes on immediately via androsta-4,16-dien-3-one 4 to androsta-4,16-diene-3,6-dione 5 , which is formed quickly in a high yield (>90%) without by-products.

Under Jones conditions this surprising reaction usually does not occur.

Unlike the steroids 1, 2, 3, and 4, the dione 5 is a new, still unknown member among the physiologically interesting 16-unsaturated C_{19} steroids. It was not mentioned in the review of Gower (4), nor has any synthesis been reported during the last few years.



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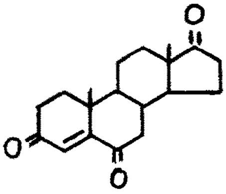

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A special property of the new dione 5 is its odor. Whereas some members (e.g., 2 and 3) do not smell, the dione 5 has a penetrating urine-like odor similar to that of the ketone 1 , the well-known boar pheromone (4). At present, the usefulness of the new dione as an artificial boar pheromone is being examined.

The dione 5 showed $\lambda_{max} = 247$ nm (log ε 3.97) in the UV spectrum. In the IR spectrum characteristic bands for the 3-keto-Δ^4-6-keto structure at 1611 , 1700 (broad), 3050, and 3064 cm^{-1} were found. In the mass spectrum (75 eV) six characteristic peaks were present: $M^+ = 284.1786$ (mol peak; calcd for the formula $C_{19}H_{24}O_2$: 284.1776), $269 = M^+ - CH_3$, $256 = M^+ - C_2H_4$, $242 = M^+ - C_3H_6$, $190 = M^+ - C_7H_{10}$, $138 = M^+ - C_{11}H_{14}$.

The ^{13}C-NMR spectrum of 5 was compared with that of androst-4-ene-3,6,17-trione 6 (5). The chemical shifts of the ring A and ring B carbon atoms of both compounds 5 and 6 are noted in Table 1 . They agree together excellently and demonstrate also the 3-keto-Δ^4-6-keto structure of the dione 5 . The results of TLC are noted in Table 2 .

Table 1: Chemical shifts (in ppm) of ring A and ring B carbon atoms of the ketones 5 and 6

carbon atom	5	6
1	35.2	35.6
2	33.7	33.8
3	198.8	199.1
4	125.4	126.0
5	160.6	160.2
6	201.4	201.2
7	46.5	45.5
8	32.6	33.9
9	51.4	51.6
10	39.7	39.7

Table 2: Results of TLC on silufol plates

steroid	R_f value [a]	uv activity	color [b]	
			hot	cold
1	0.60	–	purple	brown
2	0.23	–	dark purple	blue-black
3	0.46	+	pink	green

[a] Benzene/acetone (9 : 1) as solvent.

[b] After spraying with vanillin in sulfuric acid and heating.

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