Note

17α-acetoxy-17β-methyl-16β-phenyl-D-homo-4,6-pregnadiene-3,17α-dione: synthesis and crystal structure determination of a new rearranged pregnane derivative

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The title compound is C_{29}H_{34}O_{4}, tetragonal, P4_3, a = b = 10.310(1), c = 23.871(2) Å. The A, B, C, and D rings adopt envelope, half-chair, chair, and distorted chair conformations, respectively. The phenyl ring is planar. The methyl substituents at the A/B, C/D, and at C(17) are axial; and the — OCOC_{3}H_{3} group at C(17) and phenyl ring at C(16) are equatorial. The molecules in the crystal are held together by van der Waals forces and several C–H···O hydrogen bond interactions.

Introduction

Prostate cancer is now the most common malignancy and the second leading cause of cancer deaths in North American men. Androgen antagonists offer a potentially useful treatment for androgen mediated diseases such as: prostatic cancer, hirsutism, acne, seborrhea, androgenic alopecia and benign prostatic hyperplasia. Although surgery presently represents an alternative treatment for prostatic cancer, there are several other modalities available for the treatment of this disease. Currently the most common therapy for the treatment of androgen dependent diseases is the blockage of androgen receptors by androgen antagonists or inhibition of the conversion of testosterone to dihydrotestosterone by the enzyme 5α-reductase. This fact indicates very clearly that in this case the logical site of therapeutic intervention should be the inhibition of this enzyme. In this paper we describe the synthesis and structure determination by X-rays of 17α-acetoxy-17β-methyl-16β-phenyl-D-homo-4,6-pregnadiene-3,17α-dione. The synthesis of this compound is shown in Scheme 1. All of the synthetic steps involved in the synthesis of 9 are well-known reactions. Probably the most intriguing step in this synthesis is the hydrolysis of the ketal 5; this reaction did not afford the expected intermediate 6, but yielded the D-homo steroid 7. This D-ring expansion could be explained by protonation of the C-20 carbonyl group (perchloric acid) to form the carbonium ion 7a. A subsequent Wagner Meerwein shift of the 16,17 bond afforded compound 7 with the D-homo ring (Fig. 1).

Experimental

Suitable crystals were formed directly from the synthesis of the compound and recrystallized from ethyl acetate solution by slow evaporation of the solvent at room temperature.

The structure of the title compound was solved by the program SHELXS-86 and refined on F^2 with SHEXTL with scattering factors from International...
Fig. 1. A thermal ellipsoid plot of the molecular structure of 17α-Acetoxy-17β-methyl-16β-phenyl-D-homo-4,6-pregnadiene-3,17a-dione.