

NEW STEROIDAL HETEROCYCLES : PART XII : A SYNTHESIS OF
1,6-BISTHIABENZ[3,4]-D-HOMOESTRA-3,5(10),8,14-TETRAEN-17a-ONE

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Abstract — The synthesis of the title compound (I) from
isothiochroman-4-one (II) is reported.

Earlier¹ we pointed out that heterocyclic derivatives of steroids display different types of physiological activity, such as, anabolic, anti-inflammatory, anti-tumor, etc. Huisman^{2,3} also claimed in recent times that 6-thiaestrone derivatives were found to exhibit potent antifertility activity in mice and rats.

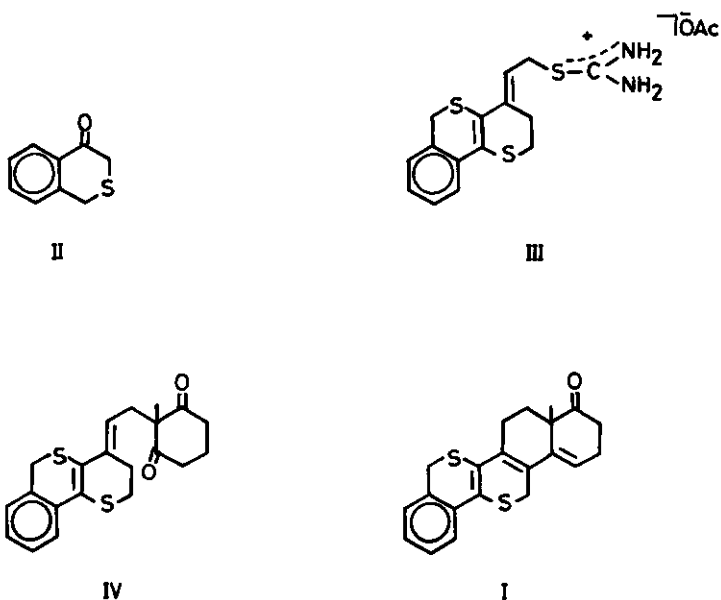
Quite recently Ghosh and Hazra⁴ have also reported the synthesis of a series of pentacyclic steroids by fusing an ethano bridge to positions 4 and 6 of estrone with the intention of studying their antifertility property.

With a view to developing newer methods to synthesize pentacyclic steroids, containing several heteroatoms in the nucleus and also to studying their physiological activity, we achieved¹ earlier the synthesis of 1,6-bisthiabenz[3,4]estra-3,5(10),8,14-tetraen-17-one.

The present report is concerned with the description of the synthesis of another pentacyclic 1,6-bisthiasteroid (I). The steps involved in the synthesis of the title compound (I) are depicted in Scheme I.

Condensation of the known isothiuronium acetate¹ (III) prepared from isothiochroman-4-one⁵ (II) with 2-methylcyclohexane-1,3-dione⁶ in a heterogeneous medium (water and ether) at room temperature afforded the D-homoseco-steroid, 8,14-seco-1,6-bisthiabenz[3,4]-D-homoestra-3,5(10),9(11)-triene-14,17a-dione (IV), as a pale yellow thick gum in 78% yield. All attempts towards solidification failed to furnish a crystalline solid; ir (CHCl₃) 1725, 1690 cm⁻¹ (characteristic of 2,2-disubstituted⁷ cyclohexane-1,3-dione moiety); nmr δ (CDCl₃) 1.22 (3H, s, C₁₈-methyl), 1.6-2.1 (2H, m, methylene at C₁₆), 2.4-3.1 (10H, m, methylenes at C₇, C₈, C₁₂, C₁₅ and C₁₇), 3.6 (2H, s,

SCHEME I



methylene at C₂), 5.98 (1H, t, $\underline{J}$ 8 Hz, olefinic proton at C₁₁), 7.0-7.8 (4H, m, aromatic).

Cyclodehydration of (IV) with p-toluenesulfonic acid-benzene was successfully completed in 15 min affording the anticipated D-homobisthiasteroid (I) as a yellowish brown solid which on crystallization from acetone-methanol gave the analytical sample of the compound (I) as a dark yellow crystalline solid, mp 164-169°C, in 85% yield; ir (CHCl₃) 1695 cm⁻¹ (C = O); nmr δ (CDCl₃) 1.25 (3H, s, C₁₈-methyl), 1.3-3.0 (8H, m, methylenes at C₁₁, C₁₂, C₁₆ and C₁₇), 3.52 (2H, AB-quartet, $\underline{J}$ 15 Hz, methylene at C₇), 3.82 (2H, s, methylene at C₂), 6.18 (1H, t, $\underline{J}$ 4.5 Hz, olefinic proton at C₁₅), 7.0-7.7 (4H, m, aromatic).

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