

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.

Earlier<sup>1</sup> we pointed out that heterocyclic derivatives of steroids display different types of physiological activity, such as, anabolic, anti-inflammatory, anti-tumor, etc. Huisman<sup>2,3</sup> also claimed in recent times that 6-thiaestrone derivatives were found to exhibit potent antifertility activity in mice and rats.

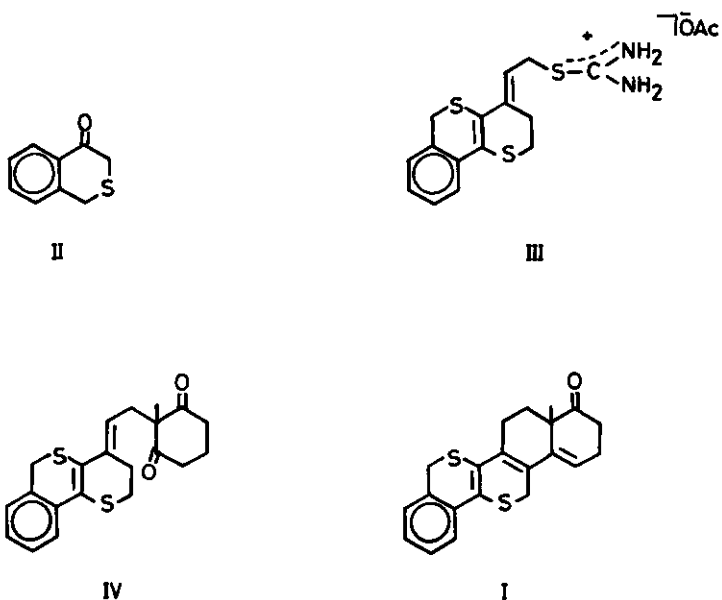
Quite recently Ghosh and Hazra<sup>4</sup> have also reported the synthesis of a series of pentacyclic steroids by fusing an ethano bridge to positions 4 and 6 of estrone with the intention of studying their antifertility property.

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 achieved<sup>1</sup> 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 acetate<sup>1</sup> (III) prepared from isothiochroman-4-one<sup>5</sup> (II) with 2-methylcyclohexane-1,3-dione<sup>6</sup> in a heterogeneous medium (water and ether) at room temperature afforded the D-homosecosteroid, 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 (CHCl<sub>3</sub>) 1725, 1690 cm<sup>-1</sup> (characteristic of 2,2-disubstituted<sup>7</sup> cyclohexane-1,3-dione moiety); nmr  $\delta$  (CDCl<sub>3</sub>) 1.22 (3H, s, C<sub>18</sub>-methyl), 1.6-2.1 (2H, m, methylene at C<sub>16</sub>), 2.4-3.1 (10H, m, methylenes at C<sub>7</sub>, C<sub>8</sub>, C<sub>12</sub>, C<sub>15</sub> and C<sub>17</sub>), 3.6 (2H, s,

SCHEME I



methylene at C<sub>2</sub>), 5.98 (1H, t,  $\underline{J}$  8 Hz, olefinic proton at C<sub>11</sub>), 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 (CHCl<sub>3</sub>) 1695 cm<sup>-1</sup> (C = O); nmr  $\delta$  (CDCl<sub>3</sub>) 1.25 (3H, s, C<sub>18</sub>-methyl), 1.3-3.0 (8H, m, methylenes at C<sub>11</sub>, C<sub>12</sub>, C<sub>16</sub> and C<sub>17</sub>), 3.52 (2H, AB-quartet,  $\underline{J}$  15 Hz, methylene at C<sub>7</sub>), 3.82 (2H, s, methylene at C<sub>2</sub>), 6.18 (1H, t,  $\underline{J}$  4.5 Hz, olefinic proton at C<sub>15</sub>), 7.0-7.7 (4H, m, aromatic).

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## REFERENCES:

1. M. Vijaya Krishna and S. R. Ramadas, Heterocycles, 1981, 16, 405.
2. H. O. Huisman, 'MTP International Review of Science', ed by W. F. Johns, Butterworths, London, 1973, Vol. 8, 236, 237.
3. J. G. Westra 'Doctorate Thesis', University of Amsterdam, 1968, p. 78.
4. A. C. Ghosh, B. G. Hazra and W. L. Duax, J. Org. Chem., 1977, 42, 3091.
5. J. V. Braun and K. Weissbach, Ber., 1929, 62, 2416.
6. M. S. Newman and A. B. Mekler, J. Am. Chem. Soc., 1960, 82, 4039.
7. H. O. Huisman, W. N. Speckamp and U. K. Pandit, Rec. Trav. Chim., Pays-Bas., 1963, 82, 898.

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