PENTACYCLIC STEROIDS, PART XVI: STUDIES ON THE TOTAL SYNTHESES OF RACEMIC 1,6-DITHIABENZ[3,4]ESTRA-3, 5(10),8,14-TETRAEN-17-ONE AND ITS D-HOMO ANALOGUE

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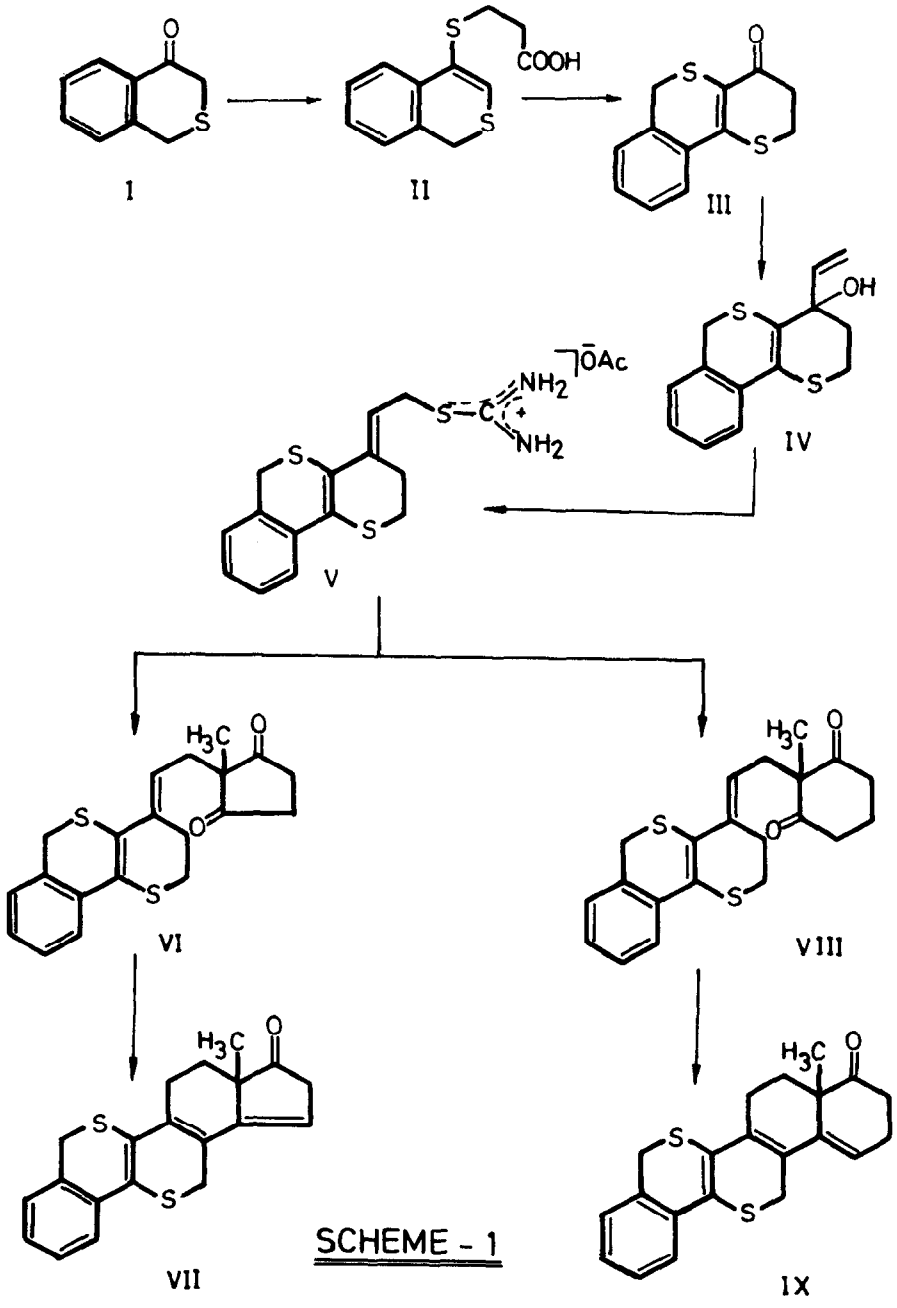
ABSTRACT

The total syntheses of racemic 1,6-dithiabenz[3,4]-estra-3,5(10),8,14-tetraen-17-one[VII] and 1,6-dithiabenz-[3,4]-D-homoestra-3,5(10),8,14-tetraen-17a-one[IX] starting from isothiochroman-4-one[I] are described.

It is well known (1,2) that the heterocyclic derivatives of steroids display different types of physiological properties such as anabolic, anti-tumor, anti-inflammatory, hypotensive, etc. Thiasteroids, such as 6-thia-8(9)-dehydroestrones, were claimed to possess anti-fertility activity(3). Moreover, pentacyclic steroids obtained by fusion of a carbocyclic ring such as benzene or cyclohexane or cyclopentane to the steroid nucleus or pentacyclic steroids derived by the fusion of a carbocyclic ring to a heterosteroid skeleton are known to exhibit interesting and diverse biological properties (4-12). Quite recently, Ghosh and Hazra (13) have also reported syntheses of a series of pentacyclic steroids by the fusion of an ethano bridge to positions 4 and 6 of estrone with the intention of studying their anti-fertility properties. A careful survey of literature (1,2,14-20) reveals the fact that there has been no report to date on the total synthesis of



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1,6-dithia pentacyclic steroids. Encouraged by this finding and also in view of our continued interest in the synthesis of newer types of thiasteroids, we wish to report, herein, the total syntheses of the racemates of the title compounds [VII] and [IX] (21).

The key intermediate, 1-oxo-4,10-dithia-1,2,3,4,9,10-hexahydrophenanthrene [III], required for the syntheses of the title compounds [VII] and [IX], was prepared starting from isothiochroman-4-one [I] (22). Isothiochroman-4-one [I], on treatment with β-mercaptopropionic acid under the catalysis of p-toluenesulfonic acid (PTS) furnished the expected β-(1H[2]benzothiopyran-4-ylthio)propionic acid [II]. Cyclodehydration of the acid [II] with phosphorus pentoxide in refluxing benzene gave the tricyclic ketone, 1-oxo-4,10-dithia-1,2,3,4,9,10-hexahydrophenanthrene [III]. The tricyclic ketone [III], on treatment with vinylmagnesium bromide under Normant reaction conditions (23) gave the anticipated allyl alcohol, 1-hydroxy-1-vinyl-4,10-dithia-1,2,3,4,9,10-hexahydrophenanthrene [IV]. The PMR spectrum ($CDCl_3$) of the allyl alcohol [IV] indicated signals at δ 2.0-3.9 (m,5H,methylenes at C_2 and C_3 and the hydroxyl proton). The methylene protons at position 9 appeared as an AB-quartet centered at δ 3.72 (J_{AB} = 14 Hz). The complex multiplet observed at δ 5.0-6.0 for the olefinic protons was in conformity with the expected ABC pattern reported for the styrene-type systems (24).

The unstable allyl alcohol [IV] reacted smoothly with thiourea and glacial acetic acid (25) affording the more stable 4,10-dithia-1,2,3,4,9,10-hexahydrophenanthrenylideneethylisothiuronium acetate [V]. Condensation of the isothiuronium acetate [V] with 2-methylcyclopentane-1,3-dione (26) in a mixture of water and ether (1:1) gave the expected 8,14-seco-1,6-dithiabenz[3,4]estra-3,5(10),9(11)-triene-14,17-dione [VI].

Cyclodehydration of the secosteroid [VI] with methanolic hydrochloric acid (27) afforded the title compound, viz. racemic 1,6-dithiabenz[3,4]estra-3,5(10),8,14-tetraen-17-one [VII].

Condensation of the isothiuronium acetate [V] with 2-methylcyclohexane-1,3-dione (28) under the same conditions yielded 8,14-seco-1,6-dithiabenz[3,4]-D-homoestra-3,5(10),9(11)-triene-14,17a-dione [VIII].

Initial attempts to effect cyclodehydration of the secodione [VIII] employing methanolic hydrochloric acid (27) or dioxane-hydrochloric acid (29) failed to furnish the desired pentacyclic dithia-D-homosteroid [IX]. However, cyclodehydration of the secosteroid [VIII] with p-toluenesulfonic acid (PTS) in refluxing benzene for 15 min proceeded smoothly, furnishing the anticipated racemic 1,6-dithiabenz[3,4]-D-homoestra-3,5(10),8,14-tetraen-17a-one [IX] (30).

Hydrogenation of the 8,9 and 14,15-olefinic bonds in the title compounds [VII] and [IX] over 10% palladium-on-carbon was unsuccessful and the starting compounds were recovered unchanged. No absorption of hydrogen was noticed at atmospheric pressure and at room temperature or at slightly elevated pressures. The observed difficulty might perhaps be due to the deactivation of the catalyst by the sulphur present in compounds [VII] and [IX].

The tricyclic ketone [III], the key intermediate in the synthesis of the title compounds [VII] and [IX] was available in larger quantity. It was felt profitable to arrive at the appropriate reaction conditions to hydrogenate the olefinic bond in the tricyclic ketone [III], so that the knowledge could be extended to hydrogenate the olefinic bonds in the two pentacyclic compounds [VII] and [IX] referred to above.

Initially hydrogenation of the olefinic bond in the tricyclic ketone [III] was attempted with 10% palladium-on-carbon or with 30% palladium-on-carbon at atmospheric pressure and at room temperature, but with no success. Attempted chemical reduction of the olefinic bond in the tricyclic compound [III] with lithium in liquid ammonia furnished a gummy material (different from the starting ketone) which on TLC examination was found to be a mixture of several components. From a study of the spectral properties of

this material (PMR and IR) it was noticed that the ketone had suffered a carbon-sulphur bond cleavage, although the olefinic bond appeared to have undergone saturation.

Hydroboration of the olefinic bond followed by protonolysis was considered as an alternative procedure to obtain the corresponding saturated tricyclic ketone (31). Hence the tricyclic ketone [III] was treated with the trimethylamine-borane complex in dry tetrahydrofuran (THF) according to the procedure of Murray (32). Protonolysis of the resulting product was effected with propionic acid. After the usual work-up, a large amount of the tricyclic ketone [III] was recovered unreacted. A small amount of the product, left after the separation of the starting tricyclic ketone, showed in its IR spectrum the absence of carbonyl absorption. The PMR spectrum of the product indicated the presence of the olefinic protons. The failure to hydrogenate the olefinic bond in the tricyclic compound [II] under hydroboration conditions may be attributed to its tetrasubstituted nature. In view of these difficulties, further conversion of the title compounds [VII] and [IX] to the corresponding 8,9,14,15-tetrahydro derivatives, viz. 1,6-dithiabenz[3,4]estra-3,5(10)-dien-17-one and 1,6-dithiabenz-[3,4]-D-homoestra-3,5(10)-dien-17a-one could not be realised.

EXPERIMENTAL (33)

β-(1H-[2]Benzothiopyran-4-ylthio)propionic acid [II]: A sol-

ution of isothiochroman-4-one [I] (16.4 g), β-mercaptopropionic acid (10.6 g) and PTS (1.33 g) in dry benzene (200 ml) was refluxed for 20 h using a Dean-Stark water separator. The benzene solution was cooled and extracted with 2N potassium carbonate solution (4 x 60 ml). The combined aqueous alkaline extracts were cooled and neutralised with dilute hydrochloric acid (1:1) at 0° to afford a dark brown solid. This solid was filtered, washed with water and dried. Recrystallisation of the crude solid from methylene chloride-hexane after treatment with norite gave the analytical sample of [II] (20 g, 80% yield) as a brown crystalline solid, mp 110-112°; IR ($CHCl_3$) ν_{max} 3500-3200 (broad, bonded carboxylic OH stretching), 1710 (CO, acid dimer), 1500, 1480, 1450 and 1420 cm^{-1} (aromatic C=C stretch). PMR ($CDCl_3$) δ 2.5-3.0(m,4H, S-CH_2-CH_2-CO), 3.8(s,2H,Ar-CH_2-S), 6.85(s,1H, olefinic proton), 7.0-8.0(m,4H, aromatic protons) and 12.0 (s,acid proton, disappeared on D_2O exchange); CMR ($CDCl_3$) (34) δ 28.73(t,S-$\underline{CH_2}$-CH_2CO), 31.04(t,Ar-CH_2-S), 34.2(t, S-CH_2-$\underline{CH_2}$-CO), 125.62(d,olefinic carbon at position 3), 127.08, 128.06, 129.03 and 129.33 (d, aromatic carbons), 128.24, 129.52 and 132.62 (s,aromatic tertiary carbons) and 177.9 (s, acid carbonyl carbon); mass peaks at m/z 252($M^{+\cdot}$, 100%), m/z 179 (71%), m/z 147 (35%), m/z 135 (75%), m/z 115 (13%).

Anal. Calcd. for $C_{12}H_{12}O_2S_2$: C,56.14; H, 4.76%.

Found: C, 55.92; H, 4.51%.

1-Oxo-4,10-dithia-1,2,3,4,9,10-hexahydrophenanthrene [III]: A mixture of the bicyclic acid [II] (25.2 g) and phosphorus pentoxide (120 g) in dry, thiophene-free benzene (500 ml) was refluxed for 5 h. The reaction mixture was cooled and the benzene solution decanted. The reddish mass was decomposed with ice-cold water (500 ml) and extracted with benzene (3 x 60 ml). The combined benzene extracts were washed with saturated sodium bicarbonate solution (2 x 40 ml) and then with water (1 x 20 ml). The dried benzene layer was evaporated to afford the tricyclic ketone [III] as a reddish brown solid (15 g). Chromatography of this material through silica gel (250 g) furnished from benzene-hexane (2:1) eluates (4000 ml) the desired ketone [III] (7 g, 30% yield) as a brownish yellow solid, mp 148-150°. Recrystallisation from methylene chloride-hexane gave the analytical sample as a brownish yellow solid, mp 148-150°; IR ($CHCl_3$) ν_{max} 1650 (conjugated carbonyl), 1590, 1500, 1400 cm^{-1} (aromatic skeletal vibrations); PMR ($CDCl_3$) δ 2.6-3.4 (m, 4H, S-CH_2-CH_2-CO), 3.7 (s, 2H, Ar-CH_2-S), 7.0-7.8 (m, 4H, aromatic protons); CMR($CDCl_3$) (34) δ 26.18 (t, S-$\underline{CH_2}$-CH_2-CO), 30.37 (t, Ar-CH_2-S), 37.87 (t, S-CH_2-$\underline{CH_2}$-CO), 125.56, 126.74, 127.52, 131.26 (d, aromatic carbons), 128.26, 132.5, 133.22, 145.9 (s, tert-carbons) and 190.81

(s, carbonyl carbon); mass peaks at m/z 234 ($M^{+\cdot}$, 100%), m/z 233 (26%), m/z 206 (23%), m/z 178 (22%), m/z 177 (24%), m/z 146 (5%), m/z 134 (35%).

Anal. Calcd. for $C_{12}H_{10}OS_2$: C,61.54; H,4.27%.

Found: C,61.32; H,4.10%.

1-Hydroxy-1-vinyl-4,10-dithia-1,2,3,4,9,10-hexahydrophenanthrene [IV]: To a stirred suspension of vinylmagnesium bromide (from 20 ml of vinyl bromide and 3.5 g of magnesium turnings) in dry tetrahydrofuran cooled to -20° was added dropwise a solution of the tricyclic ketone [III] (4.68 g) in dry tetrahydrofuran precooled to -20° in an atmosphere of dry nitrogen. The reaction mixture was slowly brought to room temperature and then refluxed for 6 h. The dark brown Grignard complex was decomposed with ice-cold 10% ammonium chloride solution and the yellowish brown product was extracted with ether (3 x 100 ml). The dried ethereal layer was evaporated under reduced pressure to give the crude allyl alcohol [IV] (6.5 g) as a gum. Attempted purification of the product [IV] by evaporative distillation at 100-110°/ 3×10^{-4} mm led to its decomposition giving rise to a polymeric material. However, the crude allyl alcohol [IV] (6 g) on rapid chromatography through neutral alumina (120 g) furnished from methylene chloride eluates (3000 ml) a fairly pure sample of the alcohol [IV] (4.5 g, 90% yield). All attempts to induce solidification of this gum failed; IR (film) ν_{max} 3590-3100 (broad, bonded OH), 1640 (olefinic stretch), 1590, 1490, 1450 (aromatic skeletal vibrations), 1000 and 920 cm^{-1} (vinyl ending); PMR ($CDCl_3$) δ 2.0-3.9 (m, methylenes at C_2 and C_3 and the hydroxyl proton), 3.72 (AB-quartet, 2H, methylene at C_4), 5.0-6.0 (m, 3H, $-CH=CH_2$), 7.0-7.7 (m, 4H, aromatic protons).

4,10-Dithia-1,2,3,4,9,10-hexahydrophenanthrenylideneethyl-isothiuronium acetate [V]: To a mixture of the purified allyl alcohol [IV] (3.93 g) and thiourea (1.14 g) cooled to 0-5° was added 15 ml of glacial acetic acid. The resulting mixture was slowly brought to room temperature and stirred for 12 h. At the end of this period, 80 ml of dry ether was slowly added to the reaction mixture. The precipitated product was separated and washed several times with dry acetone (4 x 15 ml) to furnish the analytical sample of [V] (2.9 g, 60% yield), as a white amorphous solid, mp 138-140°; IR (KBr) ν_{max} 3240 (NH stretch), 1645 (olefinic stretch), 1580, 1500, 1470 and 1440 cm^{-1} (aromatic skeletal vibrations); PMR (DMSO-d_6) δ 1.82 (s, 3H, $OCOCH_3$), 2.6-3.4 (m, 4H, methylenes at C_2 and C_3), 3.81 [d, 2H, CH_2-S-$C(NH_2)_2$, J = 8 Hz], 3.82 (s, 2H, benzylic methylene at C_9), 6.24 (t, 1H, olefinic proton, J = 8 Hz) and 7.0-7.8 (m, 8H, aromatic and amino protons); mass peaks at m/z 278 (20%), m/z 245 (63%), m/z

243 (2%), m/z 217 (4%), m/z 212 (10%), m/z 185 (7%), m/z 179 (4%), m/z 165 (5%) and m/z 134 (5%).

Anal. Calcd. for $C_{17}H_{20}N_2O_2S_3$: C,53.68; H,5.26; N,7.37%.

Found: C,53.2; H,5.10; N,7.22%.

8,14-Seco-1,6-dithiabenz[3,4]estra-3,5(10),9(11)-triene-14,17-dione [VI]: The isothiuronium acetate [V] (0.64 g) and 2-methylcyclopentane-1,3-dione (0.23 g) were vigorously stirred in a heterogeneous medium consisting of water (10 ml) and ether (10 ml) for 6 h. The ether layer was separated and the aqueous layer was extracted with ether (2 x 20 ml). The combined ether extract was washed successively with 10% potassium carbonate solution (3 x 15 ml) and water (2 x 15 ml). Evaporation of the dried solvent afforded a thick brown gum (0.82 g) which on chromatography through neutral alumina (25 g) furnished from benzene-hexane (3:1) eluates (1500 ml) a brownish yellow solid which on recrystallisation from methanol gave the analytical sample of [VI] (0.67 g, 95% yield) as brownish yellow flakes, mp 110-112°; UV λ_{max} (ethanol) 215 (ε, 2816), 259 (ε, 2720) and 358 nm (ε, 2272); IR ($CHCl_3$) ν_{max} 1750, 1725 [characteristic of 2,2-disubstituted (35) cyclopentane-1,3-dione moiety], 1620 (trisubstituted C=C), 1480, 1450 and 1410 cm^{-1} (aromatic skeletal vibrations) PMR ($CDCl_3$) δ 1.15 (s,3H,C_{18}-methyl), 2.55 (d, 2H, methylene at C_{12}, J = 8 Hz), 2.7 (s, 4H, methylenes at C_{15} and C_{16}), 2.7-3.2 (m, 4H, methylenes at C_7 and C_8), 3.7 (s, 2H, methylene at C_2), 6.05 (t, 1H, olefinic proton at C_{11}, J = 8 Hz) and 7.1-7.9 (m, 4H, aromatic protons); CMR ($CDCl_3$) (34) δ 19.47 (q, C_{18}-methyl), 26.66 (t, methylene at C_7), 27.02 (t, methylene at C_8), 31.05 (t, methylene at C_2), 35.36 (t,methylene at C_{12}), 35.72 (t, methylenes at C_{15} and C_{16}), 56.78 (s, tert-carbon at position 13), 122.7 (d, carbon at position 11), 125.19, 125.98, 127.32 and 128.54 (d, aromatic carbons), 125.38 (s, tert-carbon at position 9), 126.65, 132.13, 134.93 and 135.54 (s, tert-carbons at C_3, C_4, C_5 and C_{10}) and 216.73 (s, carbonyl carbons at positions 14 and 17); mass peaks at m/z 356 ($M^{+\cdot}$, 33%), m/z 245 (100%), m/z 243 (3%), m/z 217 (4%), m/z 212 (24%), m/z 211 (16%), m/z 199 (7%), m/z 185 (8%), m/z 179 (6%), m/z 165 (7%), m/z 147 (7%) and m/z 134 (7%).

Anal. Calcd. for $C_{20}H_{20}O_2S_2$: C,67.42; H,5.62%.

Found: C,67.48; H,5.97%.

1,6-Dithiabenz[3,4]estra-3,5(10),8,14-tetraen-17-one [VII]: To a solution of the C-secosteroid [VI] (0.36 g) in minimum quantity of methanol (10 ml) at room temperature was added dropwise under stirring conc. hydrochloric acid until the solution became turbid. A little excess of the acid was added in order to have persistent turbidity. After stirring

the contents for a further period of 45 min, the precipitation was complete. The resulting solid was filtered and washed several times with a mixture of water and methanol (1:1). Rapid chromatography of this solid (0.35 g) through silica gel (35 g) furnished from benzene-hexane (2:1) eluates(1500 ml) a yellow solid which on recrystallisation from hexane-chloroform afforded an analytical sample of [VII] (0.26 g, 75% yield) as a yellow crystalline solid, mp 179-180°; UV λ_{max} (ethanol) 212 (ε, 13520), 218 (ε, 13182), 238 (ε, 8788), 268 (ε, 8788), 297 (ε, 9126) and 410 nm (ε,8112); IR ($CHCl_3$) ν_{max} 1735 (C=O), 1650 (trisubstituted olefinic bond), 1500, 1480, 1420 (aromatic skeletal vibrations) and 840 cm^{-1} (out of plane bending of the olefinic C-H); PMR ($CDCl_3$) δ 1.15 (s, 3H, C_{18}-methyl), 1.5-3.35 (m, 6H, methylenes at C_{11}, C_{12} and C_{16}), 3.51 (AB-quartet, 2H, methylene at C_7, J_{AB} = 14 Hz), 3.8 (s, 2H, methylene at C_2), 5.95 (t, 1H, olefinic proton at C_{15}, J = 3 Hz) and 7.1-7.8 (m, 4H, aromatic protons); CMR ($CDCl_3$) (34) δ 20.54 (q, C_{18}-methyl), 24.29 (t, methylene carbon at position 11), 25.16 (t, methylene carbon at position 7), 27.11 (t, methylene carbon at position 12), 31.31 (t, methylene carbon at position 2), 42 (t, methylene carbon at position 16), 48.92 (s, tert-carbon at position 13), 117.17 (d, carbon at position 15), 118.87 (s, carbon at position 14), 124.64, 126.11, 127.45 and 128.53 (d, aromatic carbons), 126.29, 129.09, 130.03,132.54, 133.97, 145.13 (s, tert-carbons at C_3, C_4, C_5, C_8, C_9 and C_{10}) and 218.67 (s, carbonyl carbon at position 17); mass peaks at m/z 338 ($M^{+\cdot}$, 100%), m/z 310 (42%), m/z 309 (19%) and m/z 295 (19%).

Anal. Calcd. for $C_{20}H_{18}OS_2$: C,71.01; H,5.33%.

Found: C,71.25; H,5.80%.

8,14-Seco-1,6-dithiabenz[3,4]-D-homoestra-3,5(10),9(11)-triene-14,17a-dione[VIII]: Condensation of the isothiuronium acetate[V] (1.6 g) with 2-methylcyclohexane-1,3-dione (0.63 g) was carried out exactly in the same manner as described for [VI] to furnish a dark yellow gum (1.8 g). Chromatography of this gum through neutral alumina (30 g) gave from benzene-hexane (1:1) eluates (2500 ml) a fairly pure sample of [VIII] (1.43 g, 78% yield) as a pale yellow gum. All attempts to solidify the gum were unsuccessful; IR ($CHCl_3$) ν_{max} 1725, 1690 [characteristic of 2,2-disubstituted (35) cyclohexane-1,3-dione moiety], 1620 (trisubstituted olefinic stretch), 1480, 1450, 1420 cm^{-1} (aromatic skeletal vibrations); PMR ($CDCl_3$) δ 1.22 (s, 3H, C_{18}-methyl), 1.6-2.1 (m, 2H, methylene at C_{16}), 2.4-3.1 (m, 10H, methylenes at C_7, C_8, C_{12}, C_{15} and C_{17}), 3.6 (s, 2H, methylene at C_2), 5.98 (t, 1H, olefinic proton at C_{11}, J = 8 Hz) and 7.0-7.8 (m, 4H, aromatic protons); mass peaks at m/z 370 ($M^{+\cdot}$, 20%), m/z 245 (93%), m/z 244 (100%), m/z 243 (80%), m/z 229 (17%), m/z

217 (20%), m/z 212 (21%), m/z 185 (13%) and m/z 165 (15%).

Anal. Calcd. for $C_{21}H_{22}O_2S_2$: C,68.11; H,5.94%.

Found: C,67.94; H,5.63%.

Attempted cyclodehydration of 8,14-seco-1,6-dithiabenz-[3,4]-D-homoestra-3,5(10),9(11)-triene-14,17a-dione[VIII] employing methanolic hydrochloric acid: The secosteroid [VIII](0.2 g) was subjected to cyclodehydration adopting exactly the procedure described for the preparation of [VII]. A comparative study of the TLC (benzene) and IR spectrum of the recovered material with that of the authentic secodione [VIII] indicated the identity of the two.

Attempted cyclodehydration of the secosteroid [VIII] employing dioxane-hydrochloric acid: Conc. hydrochloric acid was added dropwise to a solution of the secosteroid [VIII] (0.15 g) in dioxane (5 ml) maintained at 0-5° under stirring until the solution became turbid. After stirring for 30 min, a comparative TLC (benzene) of the reaction mixture with the starting secodione [VIII] revealed that no reaction had occurred. The reaction mixture was then warmed to 60° for 2 h with stirring. The solvent was removed under reduced pressure and the residue was extracted with ether (2 x 25 ml). The ether solution was washed successively with saturated sodium bicarbonate solution (2 x 15 ml) and water (2 x 20 ml). The dried ether extract was evaporated to furnish a gum which was found to be identical with the starting secodione [VIII] as evidenced from a comparative study of TLC and IR characteristics.

1,6-Dithiabenz[3,4]-D-homoestra-3,5(10),8,14-tetraen-17a-one[IX]: A solution of the secosteroid [VIII] (0.37 g) in dry, thiophene-free benzene (70 ml) containing PTS (0.04 g) was refluxed for 15 min, using a Dean-Stark water separator. The reaction mixture was cooled and poured over ice (40 g). The benzene layer was separated and the aqueous layer was extracted with benzene (2 x 20 ml). The combined benzene extracts were washed successively with saturated sodium bicarbonate solution (20 ml) and sodium chloride solution (2 x 15 ml). Evaporation of the dried solvent gave a crude yellow solid, which on chromatography through silica gel (30 g) furnished from benzene-hexane (3:2) eluates (1200 ml) a pure sample of [IX] (0.3 g, 85% yield). An analytical sample was obtained by recrystallisation from methanol containing a few drops of acetone, as a dark yellow crystalline solid, mp 164-169°; IR ($CHCl_3$) ν_{max} 1695 (C=O), 1610 (trisubstituted olefinic stretch), 1475, 1445 and 1420 cm^{-1} (aromatic skeletal vibrations); PMR ($CDCl_3$) δ 1.25 (s, 3H, C_{18}-methyl), 1.3-3.0 (m, 8H, methylenes at C_{11}, C_{12}, C_{16} and C_{17}), 3.52 (AB-quartet, 2H, methylene at C_7, J_{AB} = 15 Hz),

3.82 (s, 2H, methylene at C_2), 6.1 (t, 1H, olefinic proton at C_{15}, J = 4.5 Hz), 7.0-8.0 (m, 4H, aromatic protons); mass peaks at m/z 352 ($M^{+\cdot}$, 100%), m/z 351 (26%), m/z 337 (6%), m/z 335 (6%), m/z 319 (8%) and m/z 307 (5%).

Anal. Calcd. for $C_{21}H_{20}OS_2$: C,71.6; H,5.68%.

Found: C,72.05; H,5.88%.

Attempted catalytic hydrogenation of the 8,9-and 14,15-olefinic bonds in the pentacyclic compounds [VII] and [IX]: A solution of [VII] (0.1 g) in dry, thiophene-free, benzene (15 ml) was stirred with 10% palladium-on-carbon catalyst (0.1 g) in an atmosphere of hydrogen for 12 h in a Parr hydrogenator. No absorption of hydrogen was noticed at atmospheric pressure and at room temperature. The experiment was continued for a further period of 3 h at an elevated pressure of 2 to 3 atmospheres. No absorption of hydrogen was noticed. The catalyst was removed by filtration and the benzene solution was evaporated to afford a yellow solid which was found to be identical with the starting compound [VII] by a comparative study of TLC, IR and mixed mp determinations.

Attempted catalytic hydrogenation of the olefinic bond in the tricyclic ketone [III]: Catalytic hydrogenation of [III] (0.5 g) was carried out employing 10% palladium-on-carbon as well as 30% palladium-on-carbon catalysts following the procedure described above. The yellow solid obtained was found to be identical with an authentic sample of [III] by a comparative study of the TLC, IR and mixed mp determinations.

Attempted chemical reduction of the olefinic bond in [III]: To a stirred solution of the tricyclic ketone (0.5 g) in liquid ammonia (150 ml) and dry THF (50 ml) was added freshly cut lithium (45 mg). Stirring was continued until the reaction was over as indicated by the disappearance of the blue colour. After the evaporation of liquid ammonia and THF, the residual reddish brown gum was taken up in ether and washed with water (3 x 20 ml). Evaporation of the dried ether extract gave a thick brown gum (0.47 g). TLC (benzene) examination of this gum indicated it to be a mixture of several components having close R_f values; IR (film) of this product ν_{max} 1700, 1600, 1490,and 1450 cm^{-1}; PMR ($CDCl_3$) δ 2.3 (s), 2.2-3.5 (m), 7.3 (s, aromatic protons).

Attempted saturation of the olefinic bond in [III] by hydroboration-protonolysis: To a stirred solution of the tricyclic ketone (0.5 g) in dry hexane (2 ml) and dry THF (10 ml) under anhydrous oxygen-free nitrogen atmosphere was added dropwise a solution of the trimethylamine-borane complex (Aldrich chemical) (0.06 g) in dry THF (10 ml). The system

was stirred at room temperature for 2 h and was then refluxed with stirring for 12 h. At the end of this period, propionic acid (6 ml) was added to the reaction mixture and the contents were refluxed for 3 h. The solvents were removed under reduced pressure. The residual yellow gum was extracted with ether (30 ml) and the organic layer was washed with water (3 x 10 ml) and dried. Evaporation of the solvent afforded a brownish yellow gummy solid (0.55 g). TLC (benzene) examination of this product indicated several spots. The predominant spot corresponded to the starting tricyclic ketone [III] (R_f value 0.56). A careful and rapid chromatography of the above crude product through a short column of silica gel (20 g) gave mainly from the benzene eluates two fractions. The first fraction obtained from benzene (250 ml) was found to possess a different R_f value from that of the starting tricyclic ketone, while the second fraction from benzene (500 ml) was shown to be the starting tricyclic ketone [III]. The following spectral data obtained for the initial fraction clearly indicated that it was not the desired saturated tricyclic ketone; IR ($CHCl_3$) ν_{max} 1630 (weak), 1590, 1480, 1440 and 1410 cm^{-1}; PMR ($CDCl_3$) δ 2.0-3.5 (m), 4.1 (s, benzylic methylene), 5.0-6.0 (m, olefinic protons), 7.0-7.9 (m, aromatic protons).

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33. The recorded temperatures are uncorrected. Hexane unless otherwise stated, refers to the fraction boiling at 60-80°. The UV spectra were determined in spectrograde ethanol using a Carl-Zeiss spectrophotometer DMR-21. IR spectra were taken using a Perkin-Elmer grating infrared spectrophotometer, model 257, PMR spectra were recorded on Varian XL100 spectrometer using TMS as internal standard, the chemical shifts being reported in 'δ' values. The CMR spectra were obtained at 25.2 MHz in the Fourier Transform (FT) mode on Varian XL 200 and Bruker WP 60 FT NMR spectrometers. Mass spectra were recorded using MAT CH-7 and DS-55 mass spectrometers.
34. The CMR data reported for all the compounds were obtained by a study of the proton-noise decoupled spectrum as well as off-resonance spectrum.
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