# Totally Synthetic Steroid Heterocycles. Part 4.[1] A Stereoselective Synthesis of 16-Thia-D-homoestradiol 3-Methyl Ether and Related Studies †

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Both a successful total synthesis of the title compound and related work are described. Two synthetic approaches have been studied utilizing the intermediate precursors, 16-thia-D-homoestra-1,3,5(10),8,14-pentaenes (1) and 9-oxo-16-thia-9,10-seco-D-homoestra-1,3,5(10),8(14)-tetraenes (15). The key steps involve double-bond reduction of these compounds. Catalytic hydrogenation and metal–ammonia reduction frequently lead to a similar unexpected ring contraction. The rearrangement, which is also examined on a bicyclic C/D model system, can be interpreted in terms of neighbouring sulphur participation. The successful route is opened up by controlled catalytic hydrogenation of the intermediates (1) and (15). Acid-catalyzed ring closure and successive reduction of the styrenoid double bond complete the stereoselective synthesis.

OUR interest in the biological properties of modified steroids has recently been directed to the total synthesis of novel 16-thia-D-homoestrogens. We now describe a complete synthesis of the title compound and related investigations. The key intermediate precursors, 16-thia-D-homoestra-1,3,5(10),8,14-pentaenes (1) and 9-oxo-16-thia-9,10-seco-D-homoestra-1,3,5(10),8(14)-tetraenes (15) have previously [2,3] been synthesized in a few steps from 2-methyl-5-thiacyclohexane-1,3-dione.

*Approach via 16-Thia-D-homoestrapentaenes.*—Our first approach involved stepwise reduction of the diene system of 16-thia-D-homoestrapentaenes (1) in a desired *trans,anti,trans* B/C/D arrangement.

Initially, we tried to reduce catalytically the 14,15-double bond. However, the estrapentaenes (1) proved quite resistant to hydrogenation under ordinary neutral conditions with various catalysts including palladium, platinum, or rhodium, probably due to a poisoning effect of divalent sulphur. After several trials, we found that catalytic reduction of this type of compound proceeds, though slowly, over platinum in alcohol in the presence of acetic acid and with low hydrogen pressures. Thus, a prolonged hydrogenation of the alcohol (1a) yielded two dihydro-compounds (Scheme 1). Unexpectedly, the normal reduction product (2a), whose C/D stereochemistry was later characterized as *cis* by an independent synthesis,‡ was only obtained in minor amounts. The main product proved to be a ring-contracted compound (3a). Similar ring contraction occurred predominantly in the reduction of the ketone (1c), giving the compound (3c) which was identified by the Pfitzner–Moffatt oxidation of the former compound (3a). The rearranged structure was consistent with spectral data of both compounds. Hydrogenation of the ketone (1c) further accompanied reductive desulphurization to afford a tricyclic derivative. This substance was identified as (4c) by oxidation of the sulphur-free alcohol (4a) obtained from the alcohol (1a) by Raney nickel reduction. Neighbouring-sulphur participation appears to be responsible for the ready ring contraction. The skeletal rearrangement may be explained by assuming an episulphonium ion intermediate (ii). This species would be formed as a result of stabilization of the incipient carbonium ion (i) generated on initial protonation at C(15), eventually undergoing the C(15)–S bond cleavage. The corresponding sulphoxides and sulphones were also examined for catalytic reduction. It was expected that the presence of an oxide or dioxide function should activate the conjugated double bond and at the same time annul sulphur participation to prevent the skeletal rearrangement. However, hydrogenation of the sulphoxides (1) (SO in place of S) caused a loss of the oxide function at earlier stages, resulting in only recovery of the parent sulphides. On the other hand, hydrogenation of the sulphones (5) was found to proceed normally at room temperature and atmospheric pressure. With platinum oxide, the sulphones (5a) and (5c) gave the corresponding dihydro-compounds (6a) and (6c) as major product, respectively. The same C/D *cis*-fusion of these products was shown by peracid oxidation of the foregoing compounds (2a) and (2c). When the sulphone (5c) was hydrogenated over 10% palladium–charcoal, a different dihydro-isomer (7c) was exclusively obtained. The latter compound was also correlated to the subsequently established compound (23c),‡ thus confirming the C/D *trans*-fusion. The above results indicated that catalytic hydrogenation of the sulphone (5c) was highly stereoselective, depending on catalysts. Use of the sulphones, nevertheless, proved unpromising for our proposed synthesis, since all attempts to effect the reconversion of sulphone to sulphide were unsuccessful.

We next examined a reduction procedure based upon carbonium ion–silane hydride transfer reaction [4] which has been regarded as an alternative to catalytic hydrogenation. Thus, the estrapentaenes (1) were treated with triethylsilane (hydrogen donor) and trifluoroacetic acid (proton source) in dichloromethane at room temperature. In contrast with the catalytic hydrogenation, no ring contraction was observed in this type of reduction. And the results led to an interesting finding that the reduction course markedly depended on the 17a-substituent.

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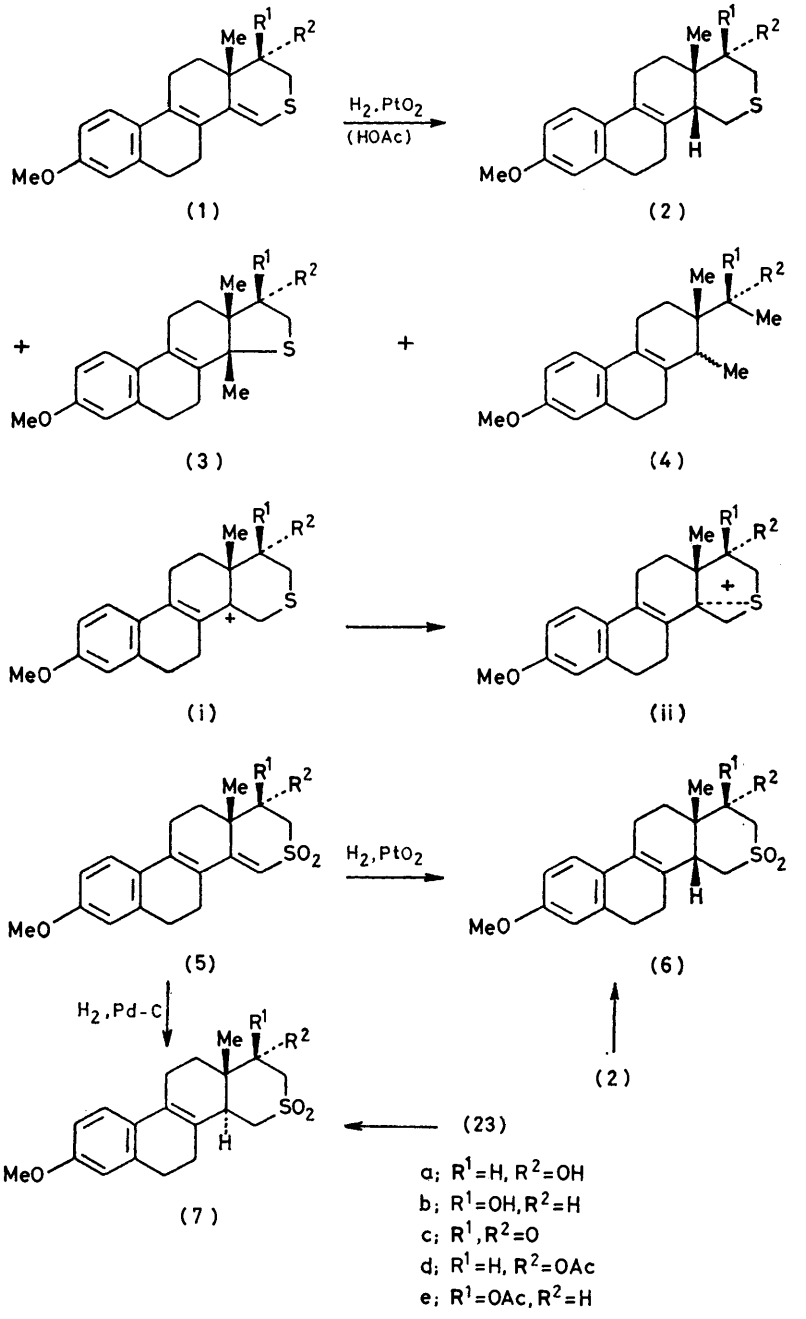
‡ The authentic samples of compounds (2) and (23) were prepared by an independent stereospecific synthesis. The work will be reported as the main subject in a subsequent paper of this series in due time. The assigned stereo-structures, based on stereospecificity of the synthetic reactions and spectral data, were finally established by *X*-ray crystallographic analysis.

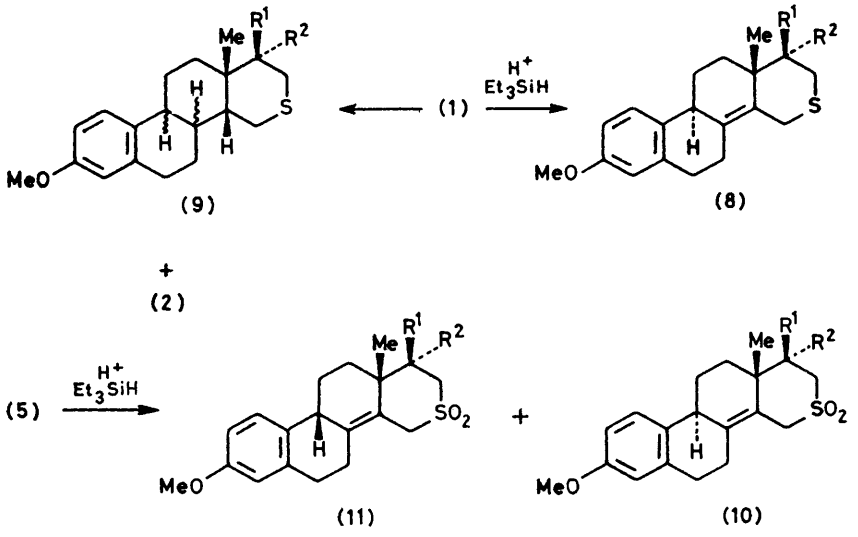
The alcohol (1a) underwent slow hydride attack, forming in 60% yield a dihydro-compound (8a) which corresponds to 1,4-addition of hydrogen (Scheme 2). The structure was consistent with its spectral data and the C(9)-configuration was assigned with regard to the sulphone derivative examination of this reaction confirmed that none of the 1,2-reduction product was detected in the reduction of the compound (1a). However, further work is needed for a rationale to explain the observed dramatic difference. Here, we failed in some attempts to induce isomerization




SCHEME 1

as described below. On the other hand, the similar reaction of the alcohol (1b) and the ketone (1c) proceeded rather rapidly to furnish a different dihydro-isomer (2b) together with a tetrahydro-compound (9b), thus indicating 1,2-reduction. The compound (2b) was proved to be a 17a-epimer of the aforementioned C/D *cis*-compound (2a) by oxidation to the same ketone (2c). A reduction of the 8,14-double bond to the 8,9-position. With respect to configurational assignment of the compound (8a), we further examined for the silane hydride reduction of the sulphones (5) which gave consistently 1,4-reduction products. The reduction of the sulphones proceeded smoothly to give a good yield of products in a shorter period compared with that of the sulphides. With 1

equiv. of triethylsilane, the sulphone (5c) gave almost quantitatively a mixture of two isomeric dihydro-compounds (10c) and (11c) which were separated in a 1.8 : 1 ratio by chromatography. Similar reaction of the sulphones (5a) and (5b) produced two pairs of isomeric compounds (10a) and (11a) (2.7 : 1 by n.m.r.) and (10b) and (11b) (1.7 : 1), respectively. These compounds were, though inseparable, identified on spectral evidence with those obtained by carbonyl reduction of the above ketones (10c) and (11c). The latter reduction led to separable mixtures of epimeric alcohols (10a) and (10b) (1.8 : 1) and (11a) and (11b) (9.4 : 1), respectively. Among them, the compound (10a) was identical with the material derived from the compound (8a) by peracid oxidation.




a; $R^1 = H$, $R^2 = OH$
b; $R^1 = OH$, $R^2 = H$
c; $R^1, R^2 = O$
d; $R^1 = H$, $R^2 = OAc$
e; $R^1 = OAc$, $R^2 = H$

SCHEME 2

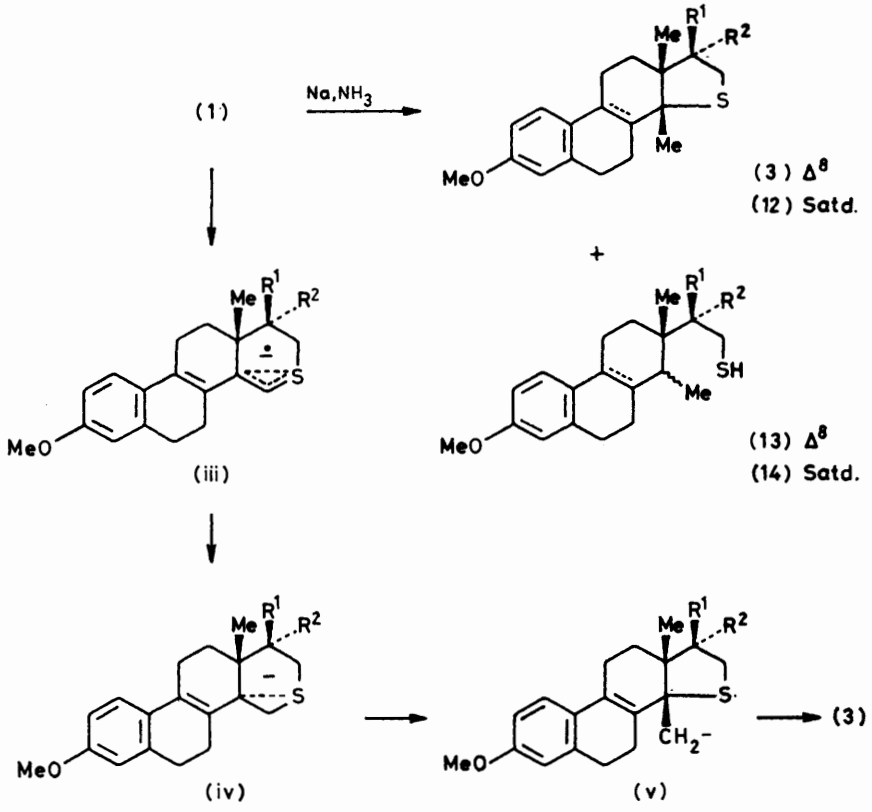
This fact suggested the same C(9)-configuration in both. We tried, unsuccessfully, with a detailed n.m.r. analysis to obtain splitting patterns for the C(9) hydrogens of an isomeric pair of the dihydro-compounds. Ultimately, the C(9) configuration in both series was tentatively assigned on the basis of a shielding effect of the 8,14 double bond on the angular group of the 9α-compound (10c) (δ 1.33) relative to the 9β-isomer (11c) (δ 1.41) from Dreiding models.

Alternatively, we also attempted metal–ammonia reduction of the estrapentaenes (1).[5] Unexpectedly, the reduction using sodium resulted in a complex mixture of products, from which a few undesired compounds were isolated with great difficulty. Thus, the compound (1a) formed the ring-contracted product (3a), identical with that previously obtained in the catalytic hydrogenation, together with its dihydro-derivative (12a) and a ring-cleaved compound; structure (14a) is assigned on spectral evidence (Scheme 3). An analogous rearranged compound (3b) was the only isolated product, although in minor amounts, from the reduction of the compound (1b). The ring-ruptured product presumably can be formed *via* the ring-contracted compound. In conformity with this view, the compound (3a) was known to undergo ready reductive cleavage at the homobenzylic position under similar conditions, giving the compounds (13a) and (14a). Again, sulphur participation, probably electrophilic, may be invoked. The observed ring contraction may be interpreted by assuming intermediacy of a radical anion (iii) and the anions (iv) and (v). However, there is no evidence that the other mechanistic possibilities, for instance, involving the initial C(15)–S bond fission and subsequent recyclization, can be excluded. In the event, we were unable to achieve the aim outlined in Scheme 1 utilizing the tetracyclic intermediate (1).

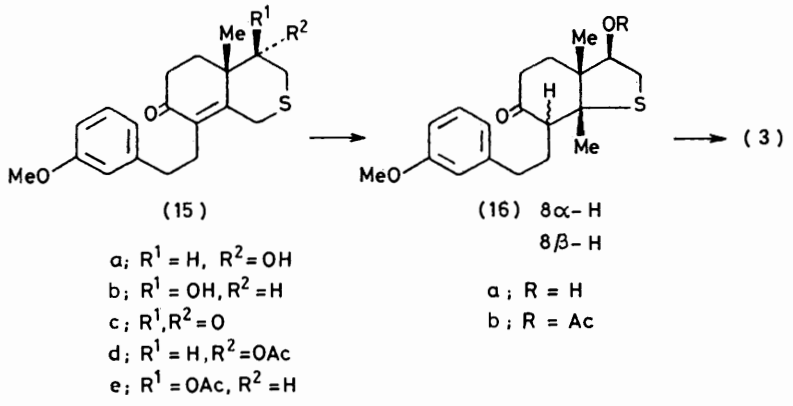
*Approach* via 9-*Oxo*-16-*thia*-9,10-*seco*-D-*homoestratetraenes*.—Our second approach proceeded from 9-oxo-16-thia-9,10-seco-D-homoestratetraenes (15) and utilized the double-bond saturation followed by the B-ring closure and successive transformations. It was expected that the conjugated double bond would be more easily reducible than the diene system of the foregoing estrapentaenes (1) and that this would allow simpler elaboration of the C/D *trans* system in such a D-homo-series. Contrary to our expectation, we again encountered some difficulties at the reduction stage.

When subjected to lithium–ammonia reduction, the ketol (15b) exclusively suffered ring contraction similar to that observed for the estrapentaenes (1) (Scheme 4).

The rearranged product (16a), obtained in 70% yield, was found to be a mixture of the 8-stereoisomers on the basis of the following evidence. Treatment of the crude acetate (16b) (1.5 : 1 mixture) with basic alumina in benzene at room temperature effected equilibration, considerably changing the isomeric ratio (6 : 1). Both isomers could be separated by chromatography. On refluxing with toluene-*p*-sulphonic acid in benzene, these compounds underwent ring closure to the same tetracyclic compound (3e), epimeric with compound (3d) already obtained. The stereo-structures of compounds (3) and, accordingly, (16) were ultimately deduced by *X*-ray crystallographic analysis on the related bicyclic system (see below). Inspection of Dreiding models

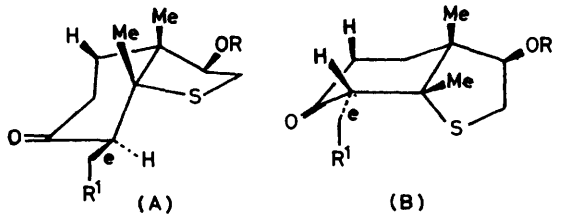



SCHEME 3




SCHEME 4

suggested the favoured conformations (A) (8α-H) and (B) (8β-H) for both isomers of the rearranged compounds

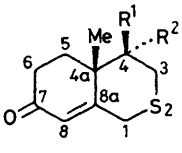


Probable conformations for both isomers of the rearranged product (16)

(16), where the alkyl side-chain would occupy a preferred equatorial position for steric reasons. On the basis of conformational considerations, conformer (A) might be expected to be more stable than conformer (B). Thus, we assigned the 8α-configuration to the major isomer and the 8β-configuration to the minor one. An apparent shielding effect ($\Delta\delta$ 0.2—0.5 p.p.m.) of the carbonyl on angular methyl group was found in the n.m.r. spectrum of the major isomer compared with the minor one. This observation was compatible with the above assignment, implying the different geometries of both ring systems.

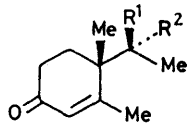
Here, in order to examine a normal reduction condition which causes no rearrangement, we undertook parallel studies on a bicyclic C/D model system. The thiadecalins (17) were prepared starting with Michael addition of methyl vinyl ketone to 2-methyl-5-thiacyclohexane-1,3-dione according to literature procedures [6,7] (Scheme 5).

On treatment with lithium in liquid ammonia and tetrahydrofuran, followed by addition of ammonium chloride, the ketol (17b) indeed yielded, exclusively, a ring-contracted compound (18b), different from the expected dihydro-derivative. The rearranged structure was supported by its spectroscopic data, the n.m.r. spectra apparently exhibiting two methyl singlets. The assigned *cis*-ring fusion was finally established by *X*-ray analysis of its acetate (18c). The analogous rearranged dione (18a), identified by oxidation of the rearranged ketol (18b), was obtained directly from the dione (17a) on Birch reduction. In this event ring fission also occurred during desulphurization to afford the monocyclic derivatives (19a) and (19b) as major products. The observed anomalous reduction can be considered as follows (Scheme 6). The initial stage in the process is probably addition of one electron in the αβ-unsaturated system to give a mesomeric radical anion (vi). A possible mechanism is that this may undergo ring contraction by ready participation of the neighbouring sulphur atom to generate a further radical anion (viii) *via* an intermediate (vii). The stereochemistry shown in the Scheme would be reasonable if the rearrangement occurred in a favoured chair conformation. The latter radical anion is able to extract a proton from the solvent ammonia and further accept a second electron. This sequence would lead *via* an enolate radical (ix) to an enolate anion (x) as the primary product. In fact, attempted enolate trapping with acetic anhydride might be expected to allow the isolation of the expected diacetate (20) in the reduction of the compound (17b). A further pathway also seems possible for formation of the same enolate anion. The starting radical anion (vi) may facilitate the initial C(1)–S bond cleavage with extrusion of the mercaptide anion to form an alternative radical anion (xi). A second electron-transfer could generate a dianion (xii) which on protonation would give the anion (xiii). The mercaptide anion moiety would then be expected to add to the new enone system, resulting in the enolate anion (x). However, it is noteworthy that the present ring contraction readily occurs without a proton source such as alcohol. This phenomenon is unlikely to be compatible with the latter mechanism. In addition, the formation of monocyclic compounds (19) from the dione (17a) would be accounted for by invoking further electron transfer to the saturated carbonyl function and subsequent C(3)–S bond fission followed by mercaptan expulsion. An analogous rearrangement has previously been reported by Leonard and Figueras [8] in the Clemensen reduction of 4-oxoisothiochroman to 1-methyl-1,2-dihydroisothionaphthene. Buchanan and Woodgate [9] also suggested 'internal participation of the sulphur atom' for the reaction mechanism.



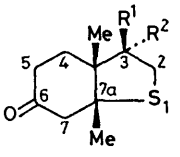
(17)

a; $R^1$, $R^2$ = O
b; $R^1$ = OH, $R^2$ = H
c; $R^1$ = H, $R^2$ = OH
d; $R^1$ = OAc, $R^2$ = H
e; $R^1$ = H, $R^2$ = OAc



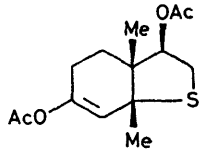
(19)

a; $R^1$, $R^2$ = O
b; $R^1$ = OH (or H), $R^2$ = H (or OH)

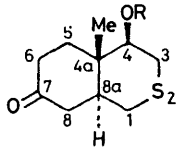


(18)

a; $R^1$, $R^2$ = O
b; $R^1$ = OH, $R^2$ = H
c; $R^1$ = OAc, $R^2$ = H



(20)



(21)

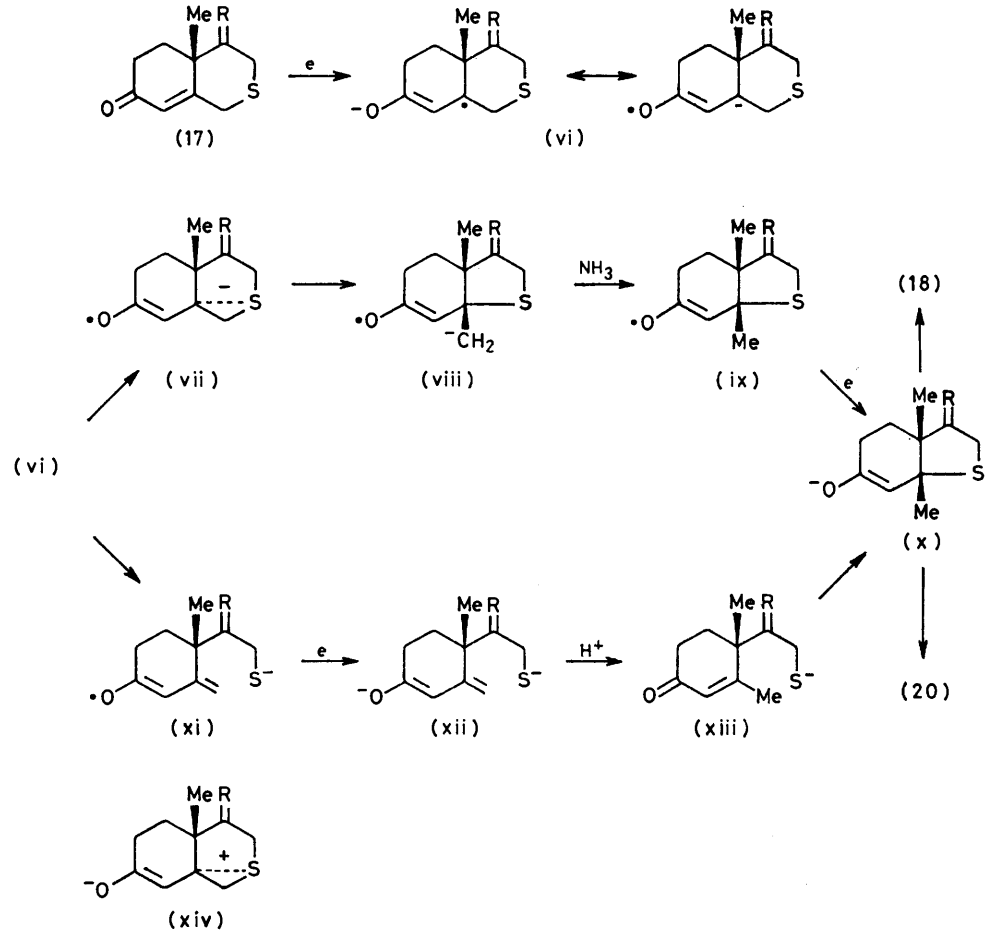
a; R = H
b; R = Ac

SCHEME 5

Alternatively, attempted catalytic hydrogenation of the substrates (17) proceeded, although sluggishly, with

palladium catalysts under neutral conditions. With 10% palladium–charcoal, however, the reduction again resulted in the same rearrangement with ring contraction; the dione (17a) gave the compounds (18a) and (19a) (14 : 1), while the ketol acetate (17d) afforded the compound (18c) as sole product. The ketol (17c) was quite resistant to catalytic reduction, the starting substrate being recovered. When the ketol (17b) was hydrogenated under similar conditions, we found that the rearranged and normal dihydro-compounds (18b) and (21a) acetate (21b), the ring fusion thus being confirmed to be favourably *trans*. Although the optimal condition for normal reduction was not further investigated in the model compounds, hydrogenation using the 5% palladium catalyst proved so effective as to be successfully applicable to the steroid precursors.

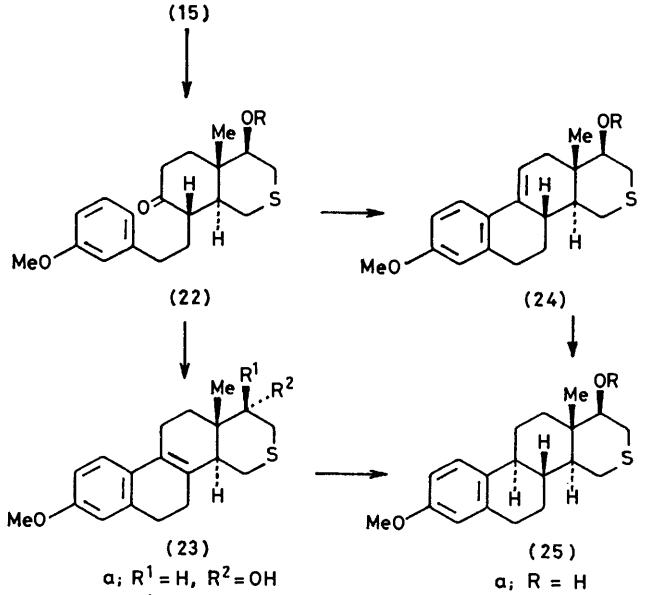
Hydrogenation of the substrates (15) was usually very slow, probably owing to steric hindrance of the alkyl side-chain. In fact, it was demonstrated that the ketol acetate (15e) was largely recovered unchanged even after




SCHEME 6

were formed in comparable amounts. Furthermore, it was known that replacement of the catalyst by 5% palladium–charcoal in this reduction required a long period for complete hydrogenation but much improved the product ratio (1 : 9.5) in favour of the latter compound. The expected product (21a) was homogeneous based on t.l.c. and n.m.r. criteria, indicating that the hydrogenation was highly stereoselective. For a similar skeletal rearrangement occurring under catalytic hydrogenation conditions, we may postulate an episulphonium ion intermediate (xiv). An explanation of the product difference depending on metal loading of the catalyst is at present not known. The stereo-structure of compound (21a) was definitely established by *X*-ray analysis of its prolonged reduction with 10% palladium–charcoal. This hydrogenation, nevertheless, gave in low yield a mixture of dihydro-products, which was composed of the rearranged and unrearranged compounds (16b) and (22b), the former isomer (Scheme 7) being favoured. When 5% palladium–charcoal was used instead, a similar reduction did not appear to proceed under neutral conditions. However, addition of acetic acid successfully caused hydrogenation to proceed without rearrangement. Thus, prolonged hydrogenation of the ketol acetate (15e) with the 5% palladium catalyst in tetrahydrofuran containing acetic acid afforded the normal dihydro-compound (22b) as a single crystalline product in moderate yield. The C/D *trans*-stereo-

chemistry was proved by subsequent transformations in accord with the above results on the bicyclic system. Also the 8β-configuration was tentatively assigned to the predominant stable isomer which caused virtually no equilibration. The crystalline acetate (22b) underwent cyclodehydration with toluene-*p*-sulphonic acid in boiling benzene, giving solely the $\Delta^8$-homoestratetraene (23e). In contrast, treatment with methanolic hydrochloric acid led to a mixture of the $\Delta^8$- and $\Delta^{9(11)}$-tetraenes (23e) and (24b) (1 : 2.6). These double-bond isomers, separable by chromatography only with difficulty, were readily differentiated by their n.m.r. signals and u.v. absorptions (263 and 276 nm) [10] associated with the presence of a styrenoid double bond. The




SCHEME 7

$\Delta^8$-isomer (23e) was chemically correlated to its 17α-epimer (23d) by oxidation of both corresponding alcohols (23a) and (23b) to the same ketone (23c). The stereo-structure of the latter acetate (23d) was determined by the *X*-ray crystallographic study, the C/D stereochemistry of the tetraenes (23) and (24) being completely verified. When a crude product from the hydrogenation of the compound (15e) was directly submitted to acid-catalyzed cyclization, a very small amount of the 14β-tetraene (2e) was also isolated as the second product. Consequently, hydrogenation of the compound (15e) is suggested to be highly stereoselective. Finally, the isomeric tetraenes (23e) and (24b) both gave, on lithium–ammonia reduction, the same estradiol derivatives (25a) and (25b). The proper *trans,anti,trans* arrangement was ascertained on the basis of spectral evidence [11] by analogy with the steroid generalization. Thus, the total synthesis of 16-thia-D-homoestradiol 3-methyl ether and its derivatives was accomplished in a five- or six-step sequence starting from 2-methyl-5-thiacyclohexane-1,3-dione.

## EXPERIMENTAL

M.p.s were determined on a calibrated Kofler hot-stage apparatus. I.r. spectra were recorded on a JASCO–DS–403G spectrophotometer and u.v. spectra on a Hitachi EPS–3T spectrophotometer. N.m.r. spectra were taken on a Varian A–60 instrument using tetramethylsilane as the internal standard. Mass spectra were determined using a Hitachi RMU–6 mass spectrometer (70 eV). Preparative t.l.c. was carried out on 100 × 20 × 0.075 or 20 × 20 × 0.2 cm glass plates coated with silica gel $GF_{254}$ (type 60; Merck). Preparative high-performance liquid chromatography (h.p.l.c.) was performed using a silica gel 60-prepacked column for liquid chromatography (size B; Merck). Alumina used for column chromatography refers to the activity grade I, neutral variety manufactured by M. Woelm, Eschwege, Germany, and made up to activity grade II by the addition of 3% water prior to use. Work-up means washing of the extracts with water and then brine, drying ($Na_2SO_4$), filtration, and evaporation under reduced pressure. Ether refers to diethyl ether.

*Catalytic Hydrogenation of Thiaestrapentaenes* (1).—(a) A solution of 3-methoxy-16-thia-D-homoestra-1,3,5(10),8,14-pentaen-17aα-ol (1a) (943 mg, 3 mmol) in ethanol–acetic acid (3 : 1; 120 ml) was hydrogenated over platinum oxide (1.9 g) at room temperature under 5 atm of hydrogen. After shaking for 72 h, 1 equiv. of hydrogen was consumed. The solution was filtered free from the catalyst and the filtrate was evaporated. The crude product was purified by preparative t.l.c. [benzene–ethyl acetate (20 : 1) with double development] which separated two components. The major one (less polar) (345 mg) gave, on trituration with ether–light petroleum, 3-*methoxy*-14β-*methyl*-15-*thia*-14β-*estra*-1,3,5(10),8-*tetraen*-17α-*ol* (3a) (281 mg), m.p. 135—140 °C. Recrystallization from the same solvent afforded an analytical specimen, m.p. 139—141 °C, $\nu_{max.}$ (dilute $CCl_4$) 3 632, 3 610sh (free OH), and 3 547sh $cm^{-1}$ (bonded OH); $\nu_{max.}(CHCl_3)$ 3 600 (OH), 1 607, 1 570, and 1 497 $cm^{-1}$ (styrene); $\lambda_{max.}$(EtOH) 282 nm (ε 16 900); δ($CDCl_3$) 1.07 (3 H, s, 13-Me), 1.42 (3 H, s, 14-Me), 3.78 (3 H, s, OMe) 4.30 (1 H, q, *J* 10 and 7 Hz, 17β-H), and 6.6—7.5 (3 H, m, ArH) (Found: C, 71.75; H, 7.7; S, 9.9. $C_{19}H_{24}O_2S$ requires C, 72.1; H, 7.65; S, 10.15%). The *acetate* (3d) was prepared with acetic anhydride and pyridine by an ordinary procedure as a crystalline solid, m.p. 153—156 °C (ether–light petroleum), $\nu_{max.}(CHCl_3)$ 1 730, 1 745 (OAc), 1 608, 1 570, and 1 497 $cm^{-1}$ (styrene); $\lambda_{max.}$(EtOH) 282 nm (ε 18 500); δ($CDCl_3$) 1.03 (3 H, s, 13-Me), 1.46 (3 H, s, 14-Me), 2.10 (3 H, s, OAc), 3.78 (3 H, s, OMe), and 5.34 (1 H, q, *J* 10 and 7.5 Hz, 17β-H) (Found: C, 70.35; H, 7.3; S, 9.15. $C_{21}H_{26}O_3S$ requires C, 70.35; H, 7.3; S, 8.95%). The minor one (124 mg) gave, on trituration with ether–light petroleum, 3-*methoxy*-16-*thia*-D-*homo*-14β-*estra*-1,3,5(10),8-*tetraen*-17aα-*ol* (2a) (35 mg), m.p. 163—166 °C (ether–light petroleum), $\nu_{max.}(CHCl_3)$ 3 575, 3 430 (OH), 1 606, 1 570, and 1 495 $cm^{-1}$ (styrene); $\lambda_{max.}$(EtOH) 277 nm (ε 19 700); *m/e* 316 ($M^+$), which was identical with an authentic sample (m.p. 169—171 °C) obtained by an alternative method.

(b) As described above, 3-*methoxy*-16-*thia*-D-*homoestra*-1,3,5(10),8,14-*pentaen*-17a-*one* (1c) (300 mg, 0.96 mmol) was hydrogenated (23 h) over platinum oxide (150 mg) in ethanol–acetic acid (3 : 1; 45 ml) until 1 equiv. of hydrogen

was consumed. Similarly, the crude product was subjected to preparative t.l.c. to afford two fractions. The less-polar one (232 mg) gave, on trituration with ether–pentane, crystalline 3-*methoxy*-14β-*methyl*-15-*thia*-14β-*estra*-1,3,5(10),8-*tetraen*-17-*one* (3c) (57 mg), m.p. 98—101 °C. Recrystallization from dichloromethane–ether provided an analytical sample, m.p. 101—103 °C, $\nu_{max.}$($CHCl_3$) 1 733 (CO), 1 611, 1 571, and 1 501 $cm^{-1}$ (styrene); $\lambda_{max.}$(EtOH) 280.5 (ε 18 400); δ($CDCl_3$) 1.22 (3 H, s, 13-Me), 1.45 (3 H, s, 14-Me), 3.78 (3 H, s, OMe), and 6.6—7.3 (3 H, m, ArH) (Found: C, 72.6; H, 7.05; S, 10.05. $C_{19}H_{22}O_2S$ requires C, 72.55; H, 7.05; S, 10.2%). The polar one (34 mg) was triturated with ether–light petroleum to give 2-*acetyl*-7-*methoxy*-1,2-*dimethyl*-1,2,3,4,9,10-*hexahydrophenanthrene* (4c) (8 mg) as a crystalline solid, m.p. 97—101 °C, $\nu_{max.}$($CHCl_3$) 1 704sh, 1 697 (CO), 1 606, 1 572, and 1 497 $cm^{-1}$ (styrene); $\lambda_{max.}$(EtOH) 272.5 nm (ε 15 900); δ($CDCl_3$) 0.90 (3 H, s, 2-Me), 1.10 (3 H, d, *J* 7 Hz, 1-Me), 2.25 (3 H, s, COMe), 3.80 (3 H, s, OMe), and 6.6—7.3 (3 H, m, ArH); *m/e* 284 ($M^+$). In another experiment, when the ketone (1c) (300 mg) was hydrogenated (15 h) in acetic acid only, *the ring-contracted product* (3c) (207 mg), m.p. 98—101 °C, was obtained as the sole product.

(c) A solution of the alcohol (1a) (63 mg, 0.2 mmol) in ethanol (10 ml) was hydrogenated (51 h) over Raney nickel (*ca.* 60 mg) at room temperature and 5 atm of hydrogen. The crude product solidified on trituration with dichloromethane–ether to give crystalline 1,2-*dimethyl*-2-(1-*hydroxyethyl*)-7-*methoxy*-1,2,3,4,9,10-*hexahydrophenanthrene* (4a) (16 mg), m.p. 88—93 °C. An analytical specimen was obtained by recrystallization from ethanol–ether, m.p. 99—101 °C, $\nu_{max.}$($CHCl_3$) 3 600 (OH), 1 607, 1 572, and 1 496 $cm^{-1}$ (styrene); $\lambda_{max.}$(EtOH) 273 nm (ε 15 300); δ($CDCl_3$) 0.85 (3 H, s, 2-Me), 1.12 (3 H, d, *J* 7 Hz, 1-Me), 1.18 [3 H, d, *J* 6.5 Hz, 2-CH(OH)Me], 3.78 (3 H, s, OMe), and 6.6—7.2 (3 H, m, ArH).

*Catalytic Hydrogenation of Thiaestrapentaene Dioxides* (5).—(a) A solution of 3-methoxy-16-thia-D-homoestra-1,3,5(10),8,14-pentaen-17aα-ol 16,16-dioxide (5a) (645 mg, 1.86 mmol) in ethanol–acetic acid (3 : 1) (560 ml) was hydrogenated over platinum oxide (1.29 g) at room temperature and atmospheric pressure. After 2.5 h, 1 equiv. of hydrogen had been consumed. The catalyst was filtered off and the solvent removed from the filtrate. The residue was purified by preparative t.l.c. [benzene–ethyl acetate (9 : 1) with triple development] to afford a major fraction (352 mg) which solidified on trituration with chloroform–ether, m.p. 236—245 °C. Two recrystallization from dichloromethane–ether gave pure 3-*methoxy*-16-*thia*-D-*homo*-14β-*estra*-1,3,5(10),8-*tetraen*-17aα-*ol* 16,16-*dioxide* (6a), m.p. 254—255 °C, $\nu_{max.}$($CHCl_3$) 3 500 (OH), 1 606, 1 571, and 1 497 $cm^{-1}$ (styrene); $\lambda_{max.}$(EtOH) 275 nm (ε 15 200); *m/e* 348 ($M^+$) (Found: C, 65.1; H, 6.85; S, 9.2. $C_{19}H_{24}O_4S$ requires C, 65.5; H, 6.95; S, 9.2%). This material was identical with that derived from the above compound (2a) by oxidation with *m*-chloroperbenzoic acid.

(b) A solution of 3-methoxy-16-thia-D-homoestra-1,3,5(10),8,14-pentaen-17a-one 16,16-dioxide (5c) (100 mg in ethanol–acetic acid (3 : 1; 100 ml) was hydrogenated (4 h) over platinum oxide (200 mg) as described above. The crude product was purified by preparative t.l.c. [benzene–ethyl acetate (9 : 1) with triple development] which afforded as a major fraction crystalline 3-*methoxy*-16-*thia*-D-*homo*-14β-*estra*-1,3,5(10),8-*tetraen*-17a-*one* 16,16-*dioxide* (6c) (40 mg), m.p. 176—185 °C (dichloromethane–ether). The pure material was obtained by recrystallization from dichloromethane–ether, m.p. 183—187 °C, $\nu_{max.}$($CHCl_3$) 1 719, 1 716 (CO), 1 606, 1 570, and 1 498 $cm^{-1}$ (styrene); $\lambda_{max.}$(EtOH) 276 nm (ε 14 800); *m/e* 346 ($M^+$). This material was identified with that obtained by peracid oxidation of the compound (2c) or Pfitzer–Moffatt oxidation of the compound (6a) described above.

(c) A solution of the ketone (5c) (95 mg) in ethanol (25 ml) was hydrogenated (69 h) over 10% palladium–charcoal (95 mg). The crude product was purified by preparative t.l.c. [benzene–ethyl acetate (9 : 1) with triple development] to furnish 3-*methoxy*-16-*thia*-D-*homoestra*-1,3,5(10),8-*tetraen*-17a-*one* 16,16-*dioxide* (7c) (72 mg) as a crystalline solid, m.p. 241—247 °C (dichloromethane–ether). Recrystallization from the same solvent gave an analytical specimen, m.p. 245—248 °C, $\nu_{max.}$($CHCl_3$) 1 722 (CO), 1 607, 1 571, and 1 497 $cm^{-1}$ (styrene); $\lambda_{max.}$(EtOH) 276 nm (ε 15 400); *m/e* 346 ($M^+$) (Found: C, 65.55; H, 6.4; S, 9.4. $C_{19}H_{22}O_4S$ requires C, 65.85; H, 6.4; S, 9.25%). This material was identical with that derived from the compound (23c) by peracid oxidation. In this reduction, the same C/D *trans* dihydro-compound was solely obtained even when dimethylformamide or ethanol–acetic acid (3 : 1) was used as the solvent.

*Reduction of Thiaestrapentaenes* (1) *by Hydride Transfer.*—(a) Trifluoroacetic acid (0.8 ml) was added to a stirred solution of the alcohol (1a) (314 mg, 1 mmol) and triethylsilane (580 mg, 5 mmol) in dichloromethane (10 ml). The solution was set aside for 70 h at room temperature, then poured into ice–water, and extracted with dichloromethane. The extract was washed with water and evaporated. The residue was hydrolyzed by treatment with a slurry of potassium carbonate in aqueous methanol, then poured into cold water, and extracted with dichloromethane. The oily residue, obtained upon work-up, was purified by preparative t.l.c. [benzene–ethyl acetate (9 : 1)] to give as the sole product crystalline 3-*methoxy*-16-*thia*-D-*homoestra*-1,3,5(10),8(14)-*tetraen*-17aα-*ol* (8a) (191 mg, 60.3%), m.p. 118—120 °C (dichloromethane–ether). Recrystallization from the same solvent gave an analytical specimen, m.p. 121—124 °C, $\nu_{max.}$ (dilute $CCl_4$) 3 507 $cm^{-1}$ (bonded OH); $\lambda_{max.}$(EtOH) 278 and 283 nm (ε 2 300 and 2 200); δ($CDCl_3$) 1.10 (3 H, s, 13-Me), 3.77 (3 H, s, OMe), and 6.5—7.4 (3 H, m, ArH); *m/e* 316 ($M^+$) (Found: C, 71.8; H, 7.6; S, 10.25. $C_{19}H_{24}O_2S$ requires C, 72.1; H, 7.65; S, 10.15%). The *acetate* (8d) was obtained by the established procedure as a crystalline solid, m.p. 152—155 °C (dichloromethane–ether), $\nu_{max.}$($CHCl_3$) 1 750 (OAc), 1 620, 1 581, and 1 500 $cm^{-1}$ (aromatic); $\lambda_{max.}$(EtOH) 278 and 283 nm (ε 2 000 and 1 900); δ($CDCl_3$) 1.18 (3 H, s, 13-Me), 2.15 (3 H, s, OAc), 3.79 (3 H, s, OMe), 4.84 (1 H, q, *J* 5 and 2 Hz, 17aβ-H), and 6.6—7.3 (3 H, m, ArH).

(b) To a stirred solution of the alcohol (1b) (157 mg, 0.5 mmol) and triethylsilane (0.4 ml) in dichloromethane (5 ml) was added trifluoroacetic acid (0.2 ml). The solution was set aside for 44 h and then poured into cold water, and extracted with dichloromethane. The usual work-up left an oily residue which was carefully subjected to preparative t.l.c. [benzene–ethyl acetate (9 : 1) with double development] to afford two major fractions. The less-polar one gave, on trituration with ether, 3-*methoxy*-16-*thia*-D-*homo*-14β-*estra*-1,3,5(10),8-*tetraen*-17aβ-*ol* (2b) (47 mg, 30.0%) as a crystalline solid, m.p. 139—141 °C, $\lambda_{max.}$(EtOH) 277 nm (ε 17 000); *m/e* 316 ($M^+$), identical with an authentic sample (m.p. 143—144 °C), independently prepared by an alternative

route. The polar one (24 mg, 15.1%) solidified on trituration with ether–pentane to give a *tetrahydro-compound* (9b) (24 mg, 14.9%), m.p. 170—172 °C, $\nu_{max.}$ (dilute $CCl_4$) 3 629 $cm^{-1}$ (free OH); $\lambda_{max.}$(EtOH) 279 and 287.5 nm (ε 2 000 and 1 800); *m/e* 318 ($M^+$) (Found: C, 71.3; H, 8.3; S, 10.2. $C_{19}H_{26}O_2S$ requires C, 71.65; H, 8.25; S, 10.05%). The *acetate* (9e) was prepared in the usual manner and had m.p. 169—171 °C, $\nu_{max.}$($CHCl_3$) 1 727 (OAc), 1 610, 1 580, and 1 500 $cm^{-1}$ (aromatic); δ($CDCl_3$) 1.10 (3 H, s, 13-Me), 2.07 (3 H, s, OAc), 3.78 (3 H, s, OMe), 5.47 (1 H, q, *J* 10.5 and 5 Hz, 17aα-H), and 6.6—7.3 (3 H, m, ArH).

(c) Similarly, the ketone (1c) (312 mg, 1 mmol) was reduced (4 h) using triethylsilane (3 ml) and trifluoroacetic acid (1.5 ml) in dichloromethane (20 ml). After the work-up as described above, the residue was purified by careful preparative t.l.c. [benzyl–ethyl acetate (9 : 1) with double development] which separated two major fractions. The less-polar one (68 mg, 21.6%) was crystallized from ether to give the above *dihydro-compound* (2b) (33 mg), m.p. 133—137 °C (ether–pentane). The polar one (35 mg), on trituration with ether–pentane, afforded as a crystalline solid the *tetrahydro-compound* (9b) (10 mg), m.p. 166—169 °C.

*Reduction of Thiaestrapentaene Dioxides* (5) *by Hydride Transfer*.—(a) To a stirred solution of 3-methoxy-16-thia-D-homoestra-1,3,5(10),8,14-pentaen-17a-one 16,16-dioxide (5c) (344 mg, 1 mmol) and triethylsilane (116 mg, 1 mmol) in dichloromethane (10 ml) was added trifluoroacetic acid (0.5 ml). The resulting solution was set aside for 15 h, then poured into ice–water, and extracted with dichloromethane. After work-up, the residue was subjected to preparative t.l.c. [benzene–ethyl acetate (9 : 1) with double development] which separated two fractions. The major one (less polar) (226 mg) solidified on trituration with ether, m.p. 173—175 °C (169 mg). Recrystallization from methanol gave pure *3-methoxy-16-thia-D-homoestra-1,3,5(10),8(14)-tetraen-17a-one, 16,16-dioxide* (10c), m.p. 174—177 °C, $\nu_{max.}$($CHCl_3$) 1 723 (CO), 1 611, 1 591, 1 495 (aromatic), 1 326, and 1 120 $cm^{-1}$ ($SO_2$); $\lambda_{max.}$(EtOH) 277.5 and 282 nm (ε 2 500 and 2 300); δ($CDCl_3$) 1.33 (3 H, s, 13-Me), 3.79 (3 H, s, OMe), and 6.6—7.3 (3 H, m, ArH); *m/e* 346 ($M^+$) (Found: C, 65.75; H, 6.45; S, 9.4. $C_{19}H_{22}O_4S$ requires C, 65.85; H, 6.4; S, 9.25%). The minor one (polar) (120 mg) solidified on trituration with ether, m.p. 180—184 °C (89 mg). This material was recrystallized from methanol–dichloromethane to give pure *3-methoxy-16-thia-D-homo-9β-estra-1,3,5(10),8(14)-tetraen-17a-one 16,16-dioxide* (11c), m.p. 183—186 °C, $\nu_{max.}$($CHCl_3$) 1 721 (CO), 1 610, 1 591, 1 496 (aromatic), 1 325, and 1 123 $cm^{-1}$ ($SO_2$); $\lambda_{max.}$(EtOH) 278 and 282 nm (ε 2 200 and 2 100); δ($CDCl_3$) 1.41 (3 H, s, 13-Me), 3.75 (3 H, s, OMe), and 6.5—7.3 (3 H, m, ArH); *m/e* 346 ($M^+$) (Found: C, 65.55; H, 6.4; S, 9.2. $C_{19}H_{22}O_4S$ requires C, 65.85; H, 6.4; S, 9.25%).

(b) Similarly, the sulphone (5a) (346 mg, 1 mmol) was reduced (2 h) with triethylsilane (3 ml) and trifluoroacetic acid (1.5 ml) in dichloromethane (30 ml). The major product obtained (290 mg), showing a single spot on t.l.c., was, however, found to be a 2.7 : 1 mixture of the 9α- and 9β-*isomers* (10a) and (11a) by n.m.r. spectroscopy.

(c) A hydride-transfer reaction with the sulphone (5b) (173 mg, 0.5 mmol) was also carried out (2 h) using triethylsilane (2 ml) and trifluoroacetic acid (1 ml) in dichloromethane (20 ml). An n.m.r. spectrum of the major product (113 mg) showed it to be a 1.7 : 1 mixture of 9α- and 9β-*isomers* (10b) and (11b), which were inseparable by t.l.c. The authentic specimens of the four isomers described in (b) and (c) were prepared as follows.

*Preparation of 3-Methoxy-16-thia-D-homoestra-1,3,5(10),8(14)-tetraen-17aα- and -17aβ-ol 16,16-Dioxides* (10a *and* b).—The ketone (10c) (226 mg, 0.65 mmol) was reduced in the usual way with sodium borohydride (49 mg, 1.3 mmol) in tetrahydrofuran–ethanol (1 : 2; 45 ml). The crude product obtained was subjected to preparative t.l.c. [benzene–ethyl acetate (2 : 1)] which isolated the 17aα-*ol* (10a) (less polar) (123 mg) and the 17aβ-*ol* (10b) (polar) (68 mg) in a 1.8 : 1 ratio. Both compounds, solidified on trituration with ether, were recrystallized from dichloromethane–ether to give analytical samples. The 17aα-*ol* (10a) had m.p. 194—196 °C, $\nu_{max.}$ (dilute $CCl_4$) 3 504 $cm^{-1}$ (bonded OH); $\lambda_{max.}$ 278 and 283 nm (ε 2 000 and 1 900); δ($CDCl_3$) 1.17 (3 H, s, 13-Me), 3.79 (3 H, s, OMe), and 6.6—7.3 (3 H, m, ArH); *m/e* 348 ($M^+$). This material was identified with that prepared by peracid oxidation of the sulphide (8a) obtained above. The *acetate* (10d) was prepared by the established procedure as a crystalline solid, m.p. 198—200 °C (dichloromethane–ether), $\nu_{max.}$($CHCl_3$) 1 736 (OAc), 1 611, 1 582, 1 499 (aromatic), 1 321, and 1 127 $cm^{-1}$ ($SO_2$); $\lambda_{max.}$(EtOH) 278 and 283 nm (ε 2 000 and 1 900); δ($CDCl_3$) 1.24 (3 H, s, 13-Me), 2.14 (3 H, s, OAc), 3.79 (3 H, s, OMe), 5.04 (1 H, t, *J* 4 Hz, 17aβ-H), and 6.6—7.3 (3 H, m, ArH). The 17aβ-*ol* (10b), had m.p. 205—207 °C, $\nu_{max.}$ (dilute $CCl_4$) 3 626 $cm^{-1}$ (free OH); $\lambda_{max.}$(EtOH) 277.5 and 282.5 nm (ε 2 200 and 2 100); δ($CDCl_3$) 1.11 (3 H, s, 13-Me), 3.79 (3 H, s, OMe), and 6.6—7.3 (3 H, m, ArH); *m/e* 348 ($M^+$). The *acetate* (10e) was prepared by the usual method as a crystalline solid, m.p. 238—241 °C (dichloromethane–ether), $\nu_{max.}$($CHCl_3$) 1 741 (OAc), 1 611, 1 582, 1 499 (aromatic), 1 316, and 1 129 $cm^{-1}$ ($SO_2$); $\lambda_{max.}$(EtOH) 277.5 and 283 nm (ε 2 100 and 1 900); δ($CDCl_3$) 1.19 (3 H, s, 13-Me), 2.11 (3 H, s, OAc), 3.78 (3 H, s, OMe), 5.19 (1 H, q, *J* 9 and 6.5 Hz, 17aα-H), and 6.6—7.3 (3 H, m, ArH).

*Preparation of 3-Methoxy-16-thia-D-homo-9β-estra-1,3,5(10),8(14)-tetraen-17aα- and 17aβ-ol 16,16-Dioxides* (11a) and (11b).—The ketone (11c) (120 mg, 0.35 mmol) was reduced with sodium borohydride (26 mg, 0.69 mmol) in tetrahydrofuran–ethanol (1 : 2; 24 ml) in the usual way. T.l.c. of the crude product [benzene–ethyl acetate (2 : 1)] separated the 17aα-*ol* (11a) (less polar) (101 mg) and the 17aβ-*ol* (11b) (polar) (11 mg) in a 9.4 : 1 ratio. The major isomer (11a), solidified on trituration with ether, was recrystallized from dichloromethane–ether to give an analytical specimen, m.p. 147—149 °C, $\nu_{max.}$ (dilute $CCl_4$) 3 511 $cm^{-1}$ (bonded OH); $\lambda_{max.}$(EtOH) 278 and 282.5 nm (ε 2 100 and 2 000); δ($CDCl_3$) 1.19 (3 H, s, 13-Me), 3.79 (3 H, s, OMe), and 6.6—7.3 (3 H, m, ArH); *m/e* 348 ($M^+$). The *acetate* (11d) was prepared by the established procedure as a crystalline solid, m.p. 170—172 °C (dichloromethane–ether), $\nu_{max.}$($CHCl_3$) 1 735 (OAc), 1 610, 1 582, 1 504 (aromatic), 1 320, and 1 130 $cm^{-1}$ ($SO_2$); $\lambda_{max.}$(EtOH) 278 and 283 nm (ε 2 000 and 1 900); δ($CDCl_3$) 1.29 (3 H, s, 13-Me), 1.92 (3 H, s, OAc), 3.78 (3 H, s, OMe), 4.92 (1 H, t, *J* 4 Hz, 17aβ-H), and 6.6—7.3 (3 H, m, ArH). The *minor isomer* (11b) was obtained as a foam, $\nu_{max.}$($CHCl_3$) 3 650, *ca.* 3 420 (OH), 1 611, 1 593, 1 500 (aromatic), 1 314, and 1 130 $cm^{-1}$ ($SO_2$); δ($CDCl_3$) 1.13 (3 H, s, 13-Me), 3.78 (3 H, s, OMe), and 6.6—7.3 (3 H, m, ArH); *m/e* 348 ($M^+$).

*Birch Reduction of Thiaestrapentaenes* (1).—(a) To a stirred solution of sodium (443 mg, 19.2 mmol) in dry liquid ammonia (70 ml) was dropwise added a solution of the alcohol (1a) (275 mg, 0.87 mmol) in dry tetrahydrofuran (8 ml). Stirring was continued for 30 min, after which ammonium chloride was cautiously added until the blue colour

disappeared, and the ammonia evaporated. The residue was poured into ice–water and extracted with ether–dichloromethane (4 : 1) followed by work-up. The crude product, obtained as a viscous syrup, was subjected to preparative t.l.c. [benzene–ethyl acetate (4 : 1)] which afforded eight fractions. The second fraction (27 mg), solidified on trituration with ether–pentane to give 3-*methoxy*-16-*thia*-15,16-*seco*-D-*homo*-8ξ,9ξ,14ξ-*estra*-1,3,5(10)-*trien*-17α-*ol* (14a) (16 mg), m.p. 130—134 °C. This material was recrystallized from dichloromethane–ether for analysis, m.p. 136—139 °C, $\nu_{max.}$($CHCl_3$) *ca.* 3 500 (OH), 1 610, 1 580, and 1 500 $cm^{-1}$ (aromatic); $\lambda_{max.}$(EtOH) 279 and 288 nm (ε 2 300 and 2 000); δ($CDCl_3$) 0.98 (3 H, d, *J* 6 Hz, 14-Me), 1.04 (3 H, s, 13-Me), 3.77 (3 H, s, OMe), and 6.6—7.3 (3 H, m, ArH); *m/e* 320 ($M^+$). The *diacetate* (14d) (SAc instead of SH) was obtained in the usual way as a crystalline solid; m.p. 112—113 °C (ether–pentane), $\nu_{max.}$($CHCl_3$) 1 736 (OAc), 1 692 (SAc), 1 610, and 1 503 $cm^{-1}$ (aromatic); δ($CDCl_3$) 0.88 (3 H, s, 13-Me), 1.11 (3 H, d, *J* 6 Hz, 14-Me), 2.05 (3 H, s, OAc), 2.31 (3 H, s, SAc), 3.75 (3 H, s, OMe), 5.09 (1 H, dd, *J* 11 and 2.5 Hz, CHOAc), and 6.5—7.2 (3 H, m, ArH). The third fraction (108 mg) was further purified by preparative t.l.c. to isolate a semicrystalline fraction (15 mg) which on acetylation, gave a crude acetate as a crystalline solid, m.p. 145—147 °C (ether), $\nu_{max.}$($CHCl_3$) 1 735, 1 750 (OAc), 1 615, 1 575, and 1 500 $cm^{-1}$ (aromatic); $\lambda_{max.}$(EtOH) 282 nm (ε 15 600); δ($CDCl_3$), 1.03 (3 H, s, 13-Me), 1.48 (and 1.47) (3 H, s, 14-Me), 2.12 (and 2.09) (3 H, s, OAc), 3.80 (and 3.78) (3 H, s, OMe), 5.34 (1 H, q, *J* 10 and 7 Hz, CHOAc), and 6.6—7.3 (3 H, m, ArH); *m/e* 358 (and 360) ($M^+$). This material was identified as a 4 : 1 mixture of 14β-*methyl-estratetraene* (3a) and its 8,9-*dihydro-derivative* (12a) by n.m.r. The products from other fractions were impure and not identified.

(b) Similarly, the alcohol (1b) (314 mg, 1 mmol) was reduced with sodium (506 mg, 22 mmol) using dry tetrahydrofuran (10 ml) and dry liquid ammonia (80 ml). The crude product, obtained after work-up, was subjected to repeated preparative t.l.c. [cyclohexane–ether (2 : 1) with double development], from which the *ring-contracted product* (3b) (15 mg), m.p. 115—118 °C (ether–pentane), was obtained. Acetylation gave the *acetate* (3e) as a crystalline solid, m.p. 122—124 °C (ether–pentane), identical with an authentic sample.

*Birch Reduction of* 3-*Methoxy*-14β-*methyl*-15-*thiaestra*-1,3,5(10),8-*tetraen*-17α-*ol* (3a).—In the same way as that described above, the rearranged alcohol (3a) (158 mg, 0.5 mmol) in dry tetrahydrofuran (5 ml) was treated with sodium (253 mg, 11 mmol) in dry liquid ammonia (40 ml) and the mixture then worked up. The crude product was purified carefully by repeated preparative t.l.c. [benzene–ethyl acetate (20 : 1) with double development] which afforded a major fraction (35 mg). Two crystallizations from ether–pentane furnished the *ring-cleaved product* (14a) (10 mg) as a crystalline solid, m.p. 134—137 °C, identical with the authentic sample obtained above. The residue from the mother liquor (25 mg) was further subjected to preparative t.l.c. [cyclohexane–ether (2 : 1) with triple development] to give a purer fraction (5 mg) which was presumed to be a 1 : 1 mixture of the *tricyclic compounds* (13a) and (14a) on the basis of their n.m.r. and mass spectra, *m/e* 318 (and 320) ($M^+$).

17a-*Hydroxy*-3-*methoxy*-16-*thia*-9,10-*seco*-D-*homoestra*-1,3,5(10),8(14)-*tetraen*-9-*ones* (15a) *and* (15b) *and their Acetates* (15d) *and* (15e).—Sodium borohydride (51 mg, 1.35 mmol) was added to a stirred solution of 3-methoxy-16-thia-9,10-seco-D-homoestra-1,3,5(10),8(14)-tetraene-9,17a-dione (15c) (1.54 g, 4.66 mmol) in methanol (47 ml). Stirring was continued for 1 h at room temperature. The mixture was slowly poured into ice-cold water and extracted with dichloromethane. After work-up, the crude product was purified by preparative t.l.c. [benzene–ethyl acetate (4 : 1) with double development], giving the 17aα-*ol* (15a) (less polar) (432.9 mg, 27.9%), oily, $\nu_{max.}$ (dilute $CCl_4$) 3 500 (bonded OH) and 1 677 $cm^{-1}$ (conjugated CO) and the 17aβ-*ol* (15b) (more polar) (757.4 mg, 48.9%), oily, $\nu_{max.}$ (dilute $CCl_4$) 3 629 (free OH) and 1 676 $cm^{-1}$ (conjugated CO). These alcohols were acetylated with acetic anhydride and pyridine in the usual manner. The *acetate* (15d), had m.p. 78—79.5 °C (ether), $\nu_{max.}$($CHCl_3$) 1 746, 1 730 (OAc), 1 672 (conjugated CO), 1 601, 1 585, and 1 488 $cm^{-1}$ (aromatic); $\lambda_{max.}$(EtOH) 225 and 246 nm (ε 10 900 and 11 700); δ($CDCl_3$) 1.19 (3 H, s, 13-Me), 2.07 (3 H, s, OAc), 3.78 (3 H, s, OMe), 5.10 (1 H, q, *J* 5 and 10.5 Hz, 17a-H), and 6.6—7.8 (4 H, m, ArH). The *acetate* (15e), had m.p. 70—72 °C (ether–pentane), $\nu_{max.}$($CHCl_3$) 1 733 (OAc), 1 666, 1 610 (conjugated CO), 1 602, 1 584, and 1 490 $cm^{-1}$ (aromatic); $\lambda_{max.}$(EtOH) 222.5 and 247 nm (ε 11 100 and 12 100); δ($CDCl_3$) 1.25 (3 H, s, 13-Me), 2.09 (3 H, s, OAc), 3.78 (3 H, s, OMe), 4.92 (1 H, q, *J* 2 and 5 Hz, 17a-H), and 6.6—7.3 (4 H, m, ArH).

*Metal–Ammonia Reduction of the Ketol* (15b).—A solution of the decalolone (15b) (166 mg, 0.5 mmol) in dry tetrahydrofuran (5.5 ml) was added dropwise at −60 °C to a stirred solution of lithium (90 mg) in liquid ammonia (28 ml). After 10 min, the blue colour was discharged with ammonium chloride and the ammonia was allowed to evaporate. The residue was poured into water and extracted with ether–dichloromethane (3 : 1). After work-up, the residual product (166 mg) (7a) was directly acetylated in the usual manner. The crude acetate was purified by preparative t.l.c. [cyclohexane–ether (1 : 1)] to separate two major fractions. The less-polar fraction (80.1 mg, 42.5%) gave 17β-*hydroxy*-3-*methoxy*-14β-*methyl*-15-*thia*-9,10-*seco*-8α-*estra*-1,3,5(10)-*trien*-9-*one acetate* (16aα) as a viscous oil, $\nu_{max.}$($CHCl_3$) 1 730 (OAc), 1 715 (CO), 1 610, 1 600, 1 594, 1 584, and 1 483 $cm^{-1}$ (aromatic); δ($CDCl_3$) 1.04 (3 H, s, 13-Me), 1.10 (3 H, s, 14-Me), 2.12 (3 H, s, OAc), 3.79 (3 H, s, OMe), 5.89 (1 H, q, *J* 8 and 9 Hz, 17-H), and 6.6—7.4 (4 H, m, ArH). The more-polar fraction (52.4 mg, 27.8%) afforded its 8β-*isomer* (16aβ) as a viscous syrup, $\nu_{max.}$($CHCl_3$) 1 740 (OAc), 1 722 (CO), 1 610, 1 600, 1 594, 1 583, and 1 486 $cm^{-1}$ (aromatic); δ($CDCl_3$) 1.24 (3 H, s, 13-Me), 1.56 (3 H, s, 14-Me), 2.08 (3 H, s, OAc), 3.77 (3 H, s, OMe), 5.14 (1 H, q, *J* 3 and 7 Hz, 17-H), and 6.6—7.4 (4 H, m, ArH).

*Equilibration of the Rearranged Ketol Acetate* (16b).—A solution of the crude indanolone (16b) (1.5 : 1; 45 mg) in benzene (2 ml) was well stirred with basic alumina (Activity I; 150 mg) at room temperature for 30 h. The alumina was filtered off and the solvent evaporated off *in vacuo*. The residual oil was subjected to preparative t.l.c. [benzene–ethyl acetate (20 : 1) with triple development], from which the 8α- (less polar; 36.6 mg) and 8β-*isomers* (more polar; 5.2 mg) were obtained corresponding to a ratio of 7 : 1, respectively. The ratio was *ca.* 6 : 1, based on the n.m.r. spectrum of the equilibrium mixture.

4a,5-*Dihydro*-4a-*methyl*-1H-2-*thianaphthalene*-4,7(3H,6H)-*dione* (17a).—A stirred suspension of 2-methyl-5-thiacyclohexane-1,3-dione (10 g, 69 mmol) and freshly distilled methyl vinyl ketone (5.6 g, 80 mmol) in water (160 ml) was warmed

at 50 °C for 30 h under nitrogen. After addition of sodium chloride, the resulting emulsion was extracted with dichloromethane and worked up. The oily residue was distilled under a high vacuum, to give the adduct (13.4 g, 90.2%) as a light yellow oil, b.p. 140—143 °C (0.025 nm), which was used for the subsequent reaction, $\nu_{max.}$(CHCl)$_3$ 3 600, 3 420 (OH), 1 740sh, and 1 700 cm$^{-1}$ (CO); δ(CDCl$_3$) 1.18 and 1.38 (Me); δ(C$_6$D$_6$) 1.09 and 1.15 (Me). The adduct (13.4 g, 63 mmol) was refluxed under nitrogen with pyrrolidine (8.9 g, 125 mmol) in dry benzene (350 ml) containing toluene-*p*-sulphonic acid (233 mg) overnight. After removal of the solvent, the residue was hydrolyzed by heating at 100 °C under nitrogen in 50% acetic acid (350 ml). The mixture was concentrated, poured into cold water, and extracted with dichloromethane. After work-up, the crude product was chromatographed on alumina (Activity II; 125 g). The fractions eluted with light petroleum–benzene (1 : 1) followed by benzene were collected and evaporated. The residue was crystallized from dichloromethane–ether to afford *the dione* (17a) (5.44 g), m.p. 82—83.5°. The residue from the mother liquor of crystallization was similarly re-chromatographed on alumina (Activity I; 30 g) to give an additional crop of the *dione* (0.72 g), m.p. 81—83 °C. The overall yield from the starting dione was 45.3%. Recrystallization from dichloromethane–ether provided an analytical sample, m.p. 85—87 °C, $\nu_{max.}$(CHCl$_3$) 1 711 (CO), 1 674 and 1 614 cm$^{-1}$ (conjugated CO); $\lambda_{max.}$(EtOH) 218sh, 239, and 284 nm (ε 8 100, 10 200, and 2 700); δ(CDCl$_3$) 1.51 (3 H, s, Me), 3.23 (1 H, dd, *J* 1 and 14 Hz, 3α-H), 3.32br (1 H, d, *J* 14 Hz, 1α-H), 3.56 (1 H, d, *J* 14 Hz, 3β-H), 3.85 (1 H, dd, *J* 1.5 and 14 Hz, 1β-H), and 5.88 (1 H, d, *J* 1.5 Hz, 8-H); δ(C$_6$D$_6$) 0.83 (3 H, s, Me) and 5.55 (1 H, d, *J* 1.5 Hz, 8-H); *m/e* 196 ($M^+$) (Found: C, 60.95; H, 6.2; S, 16.5. C$_{10}$H$_{12}$O$_2$S requires C, 61.2; H, 6.15; S, 16.35%).

4β- *and* 4α-*Hydroxy*-4aβ-*methyl*-3,4,4a,5-*tetrahydro*-1H-2-*thianaphthalen*-7(6H)-*one* (17b) *and* (17c) *and their Acetates* (17d) *and* (17e).—To a stirred solution of the dione (17a) (336.2 mg, 1.7 mmol) in dry ether (15 ml) and dry tetrahydrofuran (5 ml) at 0 °C lithium tri-t-butoxyaluminium hydride (930 mg, 3.66 mmol) was added in portions. After 10 min, ice–water was added carefully and the resulting suspension was neutralized with aqueous hydrochloric acid and then extracted with ether–dichloromethane (3 : 1); the mixture was then worked up. The crude product was subjected to preparative t.l.c. [benzene–ethyl acetate (2 : 1) with triple development] which separated two fractions. From the less-polar fraction, the 4α-*epimer* (17c) (83.9 mg, 24.7%) was obtained as an oil which solidified when set aside in a refrigerator. Recrystallization from ether afforded an authentic specimen, m.p. 55—58 °C, $\nu_{max.}$ (dilute CCl$_4$) 3 502 cm$^{-1}$ (bonded OH); $\nu_{max.}$(CHCl$_3$) 1 674 and 1 620 cm$^{-1}$ (conjugated CO); $\lambda_{max.}$(EtOH) 239.5 nm (ε 6 100); δ(CDCl$_3$) 1.26 (3 H, s, Me) and 5.94 (1 H, d, *J* 1.5 Hz, 1-H) (Found: C, 60.6; H, 7.2; S, 16.05. C$_{10}$H$_{14}$O$_2$S requires C, 60.55; H, 7.1; S, 16.15%). The *acetate* (17e) was prepared in the usual way as an oil, $\nu_{max.}$(CHCl$_3$) 1 748, 1 728 (OAc), 1 678, and 1 620 cm$^{-1}$ (conjugated CO); $\lambda_{max.}$(EtOH) 236.5 nm (ε 7 100); δ(CDCl$_3$) 1.35 (3 H, s, Me), 2.13 (3 H, s, OAc), 4.91 (1 H, q, *J* 2 and 4.5 Hz, 4-H), and 5.95br (1 H, s, 8-H). From the more-polar fraction, the 4β-*epimer* (17b) (211.2 mg, 62.2%) was obtained as a crystalline solid, m.p. 107—108.5 °C (ether–dichloromethane). Recrystallization from dichloromethane–ether gave an analytical specimen, m.p. 110—111.5 °C, $\nu_{max.}$ (dilute CCl$_4$) 3 629 cm$^{-1}$ (free OH); $\nu_{max.}$(CHCl$_3$) 1 675 and 1 615 cm$^{-1}$ (conjugated CO); δ(CDCl$_3$) 1.20 (3 H, s, Me) and 5.82 (1 H, d, *J* 1 Hz, 8-H) (Found: C, 60.55; H, 7.05; S, 16.2. C$_{10}$H$_{14}$O$_2$S requires C, 60.55; H, 7.1; S, 16.15%). The acetate (17d) was obtained as a crystalline solid, m.p. 113—114° (ether–dichloromethane), $\nu_{max.}$(CHCl$_3$) 1 745, 1 727 (OAc), 1 674, and 1 617 cm$^{-1}$ (conjugated CO); $\lambda_{max.}$(EtOH) 237 nm (ε 16 900); δ(CDCl$_3$) 1.28 (3 H, s, Me), 2.10 (3 H, s, OAc), 5.05 (1 H, q, *J* 5 and 10.5 Hz, 4-H), and 5.83 (1 H, d, *J* 1 Hz, 8-H).

*Lithium–Ammonia Reduction of the Ketol* (17b).—(a) A solution of the ketol (17b) (1.25 g, 6.3 mmol) in dry tetrahydrofuran (30 ml) was added dropwise to a stirred solution of lithium (0.47 g, 68 mg-atom) in liquid ammonia (200 ml). After 5 min, ammonium chloride was added until the blue colour disappeared and then the ammonia was allowed to evaporate. The residue was extracted with ether–dichloromethane (3 : 1) and then worked up. The crude product was purified by preparative t.l.c. [ether–cyclohexane (3 : 1) with double development] to give 3β-*hydroxy*-3a,4,5,6,7,7a-*hexahydro*-3aβ,7aβ-*dimethyl*-1-*thiaindan*-6-*one* (18b) (504.8 mg, 40.0%) as a semicrystalline solid, $\nu_{max.}$ (dilute CCl$_4$) 3 629 and 3 612sh cm$^{-1}$ (free OH); $\nu_{max.}$(CHCl$_3$) 1 713 cm$^{-1}$ (CO); δ(CDCl$_3$) 1.15 (3 H, s, 3a-Me), 1.38 (3 H, s, 7a-Me), and 4.57 (1 H, t, *J* 7 Hz, 3-H); *m/e* 200 ($M^+$). The *acetate* (18c) was prepared in the usual way as a crystalline solid: m.p. 72—74 °C (light petroleum–ether), $\nu_{max.}$(CHCl$_3$) 1 724 cm$^{-1}$ (CO, OAc); δ(CDCl$_3$) 1.18 (3 H, s, 3aβ-Me), 1.39 (3 H, s, 7aβ-Me), 2.13 (3 H, s, OAc), and 5.58 (1 H, q, *J* 6 and 7 Hz, 3-H); δ(C$_6$D$_6$) 0.86 (3 H, s, 3aβ-Me), 1.16 (3 H, s, 7aβ-Me), 1.68 (3 H, s, OAc), and 5.41 (1 H, q, *J* 6 and 7 Hz, 3-H); *m/e* 242 ($M^+$) (Found: C, 59.35; H, 7.5; S, 13.25. C$_{12}$H$_{18}$O$_3$S requires C, 59.45; H, 7.5; S, 13.25%).

(b) Similarly, the ketol (17b) (49.6 mg, 0.25 mmol) was reduced with lithium (17.5 mg, 2.5 mg-atom) in liquid ammonia (20 ml) except that the ammonia was evaporated without addition of ammonium chloride. When cool the residue was immediately quenched with a solution of excess of acetic anhydride (3.5 ml) in dry tetrahydrofuran (5 ml). After the mixture had been stirred at room temperature for 30 min, ether (15 ml) was added and the insoluble salt deposited was filtered off The oily material was subjected to preparative t.l.c. [benzene–ethyl acetate (4 : 1) with double development] which afforded two major fractions. The more-polar fraction afforded the acetate (18c) (23.2 mg). The less-polar fraction gave crude 3β,6-*diacetoxy*-3a,4,5,7a-*tetrahydro*-3aβ,7aβ-*dimethyl*-1-*thiaindane* (20) (10.2 mg) as a crystalline solid, m.p. 70—73 °C, on trituration with ether. This material was essentially identical (i.r. and n.m.r.) with an authentic sample prepared from the acetate (18c) by refluxing with acetic anhydride in the presence of toluene-*p*-sulphonic acid. The pure material had m.p. 89—91 °C (ether–pentane), $\nu_{max.}$(CHCl$_3$) 1 743 (OAc) and 1 686 cm$^{-1}$ (C=C); δ(CDCl$_3$) 1.06 (3 H, s, 3aβ-Me), 1.39 (3 H, s, 7aβ-Me), 2.08 (6 H, s, OAc), 5.36br (1 H, s, 7-H), and 5.38 (1 H, q, *J* 7 and 8.5 Hz, 3-H); δ(C$_6$D$_6$) 0.92 (3 H, s, 3aβ-Me), 1.30 (3 H, s, 7aβ-Me), 1.62 (3 H, s, 3β-OAc), 1.65 (3 H, s, 6-OAc), 5.5br (1 H, s, 7-H), and 5.59 (1 H, q, *J* 7 and 8.5 Hz, 3-H) (Found: C, 58.95; H, 7.0; S, 11.45. C$_{14}$H$_{20}$O$_4$S requires C, 59.15; H, 7.1; S, 11.3%).

*Lithium–Ammonia Reduction of the Dione* (17a).—Lithium metal (82 mg, 11.9 mg-atom) was dissolved in liquid ammonia (30 ml), to which was added dropwise at −70 °C with stirring a solution of the dione (17a) (196 mg, 1 mmol) in dry tetrahydrofuran (6 ml). After 5 min, ammonium chloride was added, the ammonia was evaporated, and the residue was extracted with ether–dichloromethane

(3 : 1) and then worked up. The crude oily product was subjected to preparative t.l.c. [benzene–ethyl acetate (2 : 1)] which separated three fractions. The first fraction (41.4 mg) (least polar) crystallized when set aside. Crystallization from ether–pentane afforded pure 3a,4,7,7a-*tetrahydro*-3aβ,7aβ-*dimethyl*-1-*thiaindane*-3,6(5H)-*dione* (18a) (34.7 mg) as a sublimative crystalline solid, m.p. 170—171 °C (sealed tube); $\nu_{max.}$(CHCl$_3$) 1 737sh, 1 727, and 1 717 cm$^{-1}$ (CO); δ(CDCl$_3$) 1.25 (3 H, s, 3aβ-Me), 1.34 (3 H, s, 7aβ-Me), and 3.51 (2 H, s, 2-CH$_2$); δ(C$_6$D$_6$) 0.76 (3 H, s, 3aβ-Me), 0.86 (3 H, s, 7aβ-Me), and 2.92 (2 H, s, 2-CH$_2$); *m/e* 198 ($M^+$) (Found: C, 60.45; H, 7.15; S, 16.4. $C_{10}H_{14}O_2S$ requires C, 60.55; H, 7.1; S, 16.15%). The second fraction (58.2 mg) (less polar) furnished on distillation pure 4-*acetyl*-3,4-*dimethylcyclohex*-2-*enone* (19a) (55.2 mg) as an oil, b.p. 103 °C (1 mmHg); $\nu_{max.}$(CHCl$_3$) 1 709 (CO), 1 667, and 1 621 cm$^{-1}$ (conjugated CO); $\lambda_{max.}$(EtOH) 235.5 nm (ε 10 300); δ(CDCl$_3$) 1.41 (3 H, s, 4-Me), 1.91 (3 H, d, *J* 1 Hz, 3-Me), 2.21 (3 H, s, COMe), and 5.99 (1 H, q, *J* 1 and 2.5 Hz, 2-H); *m/e* 167 ($M^+$ + 1) (Found: C, 72.1; H, 8.55. $C_{10}H_{14}O_2$ requires C, 72.25; H, 8.5%). The third fraction (25.7 mg) (most polar) was obtained as an oil which showed $\nu_{max.}$(CHCl$_3$) 3 450 (OH), 1 660 and 1 620 cm$^{-1}$ (conjugated CO); δ(CDCl$_3$) 1.08 (d, *J* 8 Hz), 1.23 (d, *J* 6 Hz), 1.94br (s), 1.98br (s), 4.02 (q, *J* 6 Hz), and 5.92br (s); *m/e* 109 ($M^+$ − 59) and 124 ($M^+$ − 44). This material was oxidized in the usual way with 8N-chromic acid to the dione (19a) identical with that obtained above, thus being identified as 4ξ-(α-*hydroxyethyl*-3,4-*dimethylcyclohex*-2-*enone* (19b).

*Oxidation of the Ketol* (18b) *to the Dione* (18a).—The ketol (18b) (100 mg, 0.5 mmol) was dissolved in anhydrous dimethyl sulphoxide (1 ml) and benzene (1 ml) containing dry pyridine (0.06 ml) and trifluoroacetic acid (0.03 ml). After dicyclohexylcarbodi-imide (309 mg, 1.5 mmol) had been added, the resulting mixture was stirred for 3 h at room temperature. Ether (20 ml) was added followed by addition of a solution of oxalic acid dihydrate (189 mg, 1.5 mmol) in methanol (2 ml). After gas evolution had ceased, water (20 ml) was added, and the insoluble dicyclohexylurea was removed by suction. The organic phase was then washed with aqueous sodium hydrogen carbonate and the mixture worked up. The crystalline residue still contained a little dicyclohexylurea which was deposited on trituration with ether–chloroform (4 : 1) and filtered off. The crude material obtained was purified by preparative t.l.c. [benzene–ethyl acetate (2 : 1)] to afford the dione (18a) (60.9 mg, 61.5%) as a crystalline solid, m.p. 168—169 °C (ether–pentane).

*Catalytic Hydrogenation of the Dione* (17a).—A solution of the dione (17a) (196 mg, 1 mmol) in tetrahydrofuran–ethanol (1 : 1; 10 ml) was shaken with hydrogen over 10% Pd–C (200 mg) for 23 h. The catalyst was filtered off and the solvent evaporated. The residue was subjected to preparative t.l.c. [benzene–ethyl acetate (9 : 1)] which separated *compounds* (18a) (150.9 mg) and (19a) (10.8 mg).

*Catalytic Hydrogenation of the Ketol Acetate* (17d).—A solution of the ketol acetate (17d) (191 mg, 0.79 mmol) in tetrahydrofuran–ethanol (1 : 1; 8 ml) was shaken with hydrogen over 10% Pd–C (191 mg). After 24 h, the mixture was worked up as described above. The crude product was purified by preparative t.l.c. [benzene–ethyl acetate (9 : 1) with double development] to give mainly the *acetate* (18c) (126.4 mg, 65.6%) as a crystalline solid, m.p. 68—72 °C.

*Catalytic Hydrogenation of the Ketol* (17b).—(a) The ketol (17b) (50 mg, 0.25 mmol) was hydrogenated (48 h) over 10% Pd–C (50 mg) in tetrahydrofuran–ethanol (1 : 1, 10 ml) and worked up as above. The crude product was directly acetylated using acetic anhydride (0.6 ml) and dry pyridine (1 ml). The crude acetate was purified by preparative t.l.c. [benzene–ethyl acetate (20 : 1) with triple development] which separated *compounds* (18c) (18.5 mg) and (21b) (21.4 mg). These materials were identical (i.r.) with authentic samples (see below).

(b) A solution of the ketol (17b) (198.3 mg, 1 mmol) in tetrahydrofuran–ethanol (1 : 1; 20 ml) was shaken with hydrogen in the presence of 5% Pd–C (198 mg). After 48 h, the mixture was worked up as above. A portion (100 mg) of the crude product was subjected to preparative t.l.c. [cyclohexane–ether (1 : 3) with triple development] to give the semicrystalline product (55.2 mg) as a main fraction. Two crystallizations from ether–pentane furnished pure 3,4,4a,5,6,8a-*hexahydro*-4β-*hydroxy*-4aβ-*methyl*-1H-2-*thianaphthalen*-7(8H)-*one* (21a) (33 mg) as a crystalline solid, m.p. 59—61 °C, δ(CDCl$_3$) 1.09 (3 H, s, Me); *m/e* 200 ($M^+$). This material was acetylated by the standard method to give the *crystalline acetate* (21b), m.p. 157—160 °C (dichloromethane–ether). Recrystallization from the same solvent afforded an analytical sample, m.p. 160—161 °C, $\nu_{max.}$(CHCl$_3$) 1 743, 1 721, and 1 714 cm$^{-1}$ (OAc and CO); δ(CDCl$_3$) 1.16 (3 H, s, Me), 2.06 (3 H, s, OAc), 4.83 (1 H, q, *J* 4.5 and 10.5 Hz, 4-H); *m/e* 242 ($M^+$) (Found: C, 59.25; H, 7.55; S, 13.45. $C_{12}H_{18}O_3S$ requires C, 59.45; H, 7.5; S, 13.25%).

(c) A further portion (*ca.* 100 mg) of the above crude product was directly acetylated and purified by preparative t.l.c. [benzene–ethyl acetate (20 : 1) with triple development] which afforded two fractions. The more-polar fraction gave unchanged ketol (17b) (13.2 mg) whilst the less-polar fraction gave a 1 : 9.5 (n.m.r.) mixture (26.2 mg) of *compounds* (18c) and (21b).

*Catalytic Hydrogenation of the Ketol Acetate* (15e).—(a) 10% *Palladium–charcoal.* A solution of the ketol acetate (15e) (168 mg, 0.45 mmol) in ethanol–tetrahydrofuran (1 : 1; 15 ml) was shaken with hydrogen on 10% palladium–charcoal (200 mg) at room temperature for 120 h. The catalyst was filtered off, the filtrate was evaporated, and the crude product (168 mg) was subjected to preparative t.l.c. [benzene–ethyl acetate (20 : 1) with triple development] which separated four components. The starting acetate (15e) (42.7 mg) was recovered unchanged from the fourth fraction. The first and third fractions afforded the 8α- (12.1 mg) and 8β-isomers (12.0 mg) of the rearranged compound (16b), identical with authentic samples obtained above, respectively. The total yield was 19.1%, based upon the recovered starting material. The second fraction gave the normal dihydro-compound (22b) (14 mg, 11.1%), identical with its authentic sample prepared below.

(b) 5% *Palladium–charcoal* (*acetic acid*). A solution of the ketol acetate (15e) (488 mg, 1.3 mmol) in tetrahydrofuran (45 ml) containing acetic acid (0.2 ml) was hydrogenated over 5% palladium-charcoal (490 mg) at room temperature for 110 h. The mixture was worked up as above to leave an oily residue (540 mg) which was purified by preparative t.l.c. [benzene–ethyl acetate (20 : 1) with triple development]. The more-polar fraction gave starting material (15e) (132.4 mg). The less-polar fraction yielded 17aβ-*hydroxy*-3-*methoxy*-16-*thia*-9,10-*seco*-D-*homoestra*-1,3,5(10)-*trien*-9-*one acetate* (22b) (209.9 mg, 58.7% based upon recovered starting material) as a crystalline solid, m.p. 102—105 °C (ether–light petroleum). Recrystallization from ether gave an analytical sample, m.p. 107—109 °C, $\nu_{max.}$

($CHCl_3$) 1 741, 1 721 (OAc), 1 711 (CO), 1 601, 1 594, 1 585, and 1 487 $cm^{-1}$ (aromatic); δ($CDCl_3$) 1.15 (3 H, s, 13-Me), 2.03 (3 H, s, OAc), 3.74 (3 H, s, OMe), 4.76 (1 H, q, *J* 4.5 and 10.5 Hz, 17a-H), and 6.6—7.3 (4 H, m, ArH); *m/e* 376 ($M^+$) (Found: C, 66.75; H, 7.6; S, 8.65. $C_{21}H_{28}O_4S$ requires C, 67.0; H, 7.5; S, 8.5%).

3-*Methoxy*-14β-*methyl*-15-*thiaestra*-1,3,5(10),8-*tetraen*-17β-*ol Acetate* (3e).—(a) A solution of the rearranged acetate (16bα) (61.9 mg, 0.16 mmol) in dry benzene (2 ml) containing toluene-*p*-sulphonic acid (6.1 mg) was heated under reflux for 1 h. The cooled solution was poured into aqueous 5% sodium hydrogen carbonate and extracted with ether–dichloromethane. Work-up left a gummy residue (53.3 mg) which was crystallized from ether–light petroleum to give the *estratetraene* (3e) (47.7 mg, 80.9%), m.p. 115.5—120 °C. Recrystallization from ether provided an authentic specimen, m.p. 122—125 °C, $\nu_{max.}$($CHCl_3$) 1 737sh, 1 730 (OAc), 1 608, 1 593, 1 570, and 1 497 $cm^{-1}$ (aromatic); $\lambda_{max.}$(EtOH) 278 nm (17 400); δ($CDCl_3$) 1.10 (3 H, s, 13-Me), 1.44 (3 H, s, 14-Me), 2.08 (3 H, s, OAc), 3.76 (3 H, s, OMe), 5.28 (1 H, q, *J* 7 and 8.5 Hz, 17-H), and 6.6—7.3 (3 H, m, ArH); *m/e* 358 ($M^+$) (Found: C, 70.2; H, 7.2; S, 8.75. $C_{21}H_{26}O_3S$ requires C, 70.35; H, 7.3; S, 8.95%).

(b) Similarly, a solution of the rearranged acetate (16bβ) (32.9 mg, 0.087 mmol) in dry benzene (1.2 ml) containing toluene-*p*-sulphonic acid (3.3 mg) was refluxed and worked up. The crude product (27.4 mg) was crystallized from ether–light petroleum to afford the *estratetraene* (3e) (24.3 mg, 77.6%), m.p. 115—118 °C, identical with that obtained above.

3-*Methoxy*-16-*thia*-D-*homoestra*-1,3,5(10),8- *and* 1,3,5(10),9(11)-*tetraen*-17aβ-*ol Acetates* (23e) *and* (24b) *with* 3-*Methoxy*-16-*thia*-D-*homo*-14β-*estra*-1,3,5(10),8-*tetraen*-17aβ-*ol Acetate* (2e).—(a) The pure acetate (22b) (25.7 mg, 0.068 mmol) was refluxed for 1 h in dry benzene (1 ml) containing toluene-*p*-sulphonic acid (3 mg). The cooled solution was poured into aqueous sodium hydrogen carbonate and extracted with ether–dichloromethane. The extracts were combined and worked up. The crude product obtained was purified by preparative t.l.c. [benzene–ethyl acetate (20 : 1)], from which the $\Delta^8$-*homoestratetraene* (23e) (15.9 mg, mg, 65%) was obtained as a crystalline solid, m.p. 177—179 °C (ethanol–ether–light petroleum), identical with its authentic sample prepared by an independent route. The authentic sample had m.p. 180—181.5 °C, $\nu_{max.}$($CHCl_3$) 1 740, 1 724 (OAc), 1 607, 1 590, 1 570, and 1 496 $cm^{-1}$ (styrene); $\lambda_{max.}$(EtOH) 276 nm (ε 18 500); δ($CDCl_3$) 0.91 (3 H, s, 13-Me), 2.07 (3 H, s, OAc), 3.78 (3 H, s, OMe), 4.89 (1 H, br q, *J* 6.5 and 10 Hz, 17a-H), and 6.6—7.3 (3 H, m, ArH); *m/e* 358 ($M^+$) (Found: C, 70.15; H, 7.25; S, 8.8. $C_{21}H_{26}O_3S$ requires C, 70.35; H, 7.3; S, 8.95%).

(b) Similarly, the crude acetate (32.4 mg) from the mother-liquor of crystallization was refluxed (2 h) in benzene (1.2 ml) containing toluene-*p*-sulphonic acid (4.3 mg) and worked up. The product was subjected to preparative t.l.c. (benzene with triple development) which separated more of the 14α-*tetraene* (23e) (less polar) (8 mg), m.p. 175—178 °C (ether–light petroleum) together with the 14β-*tetraene* (2e) (more polar) (6.4 mg), m.p. 144—147 °C (ether). The latter compound was identical with an authentic sample prepared independently, which had m.p. 149—151 °C, $\nu_{max.}$($CHCl_3$) 1 738sh, 1 726 (OAc), 1 606, 1 592, 1 572, and 1 496 $cm^{-1}$ (styrene); $\lambda_{max.}$(EtOH) 277 nm (ε 19 300); δ($CDCl_3$) 1.01 (3 H, s, 13-Me), 2.12 (3 H, s, OAc), 3.79 (3 H, s, OMe), 4.88br (1 H, t, *J* 5 Hz, 17a-H), and 6.6—7.3 (3 H, m, ArH); *m/e* 358 (Found: C, 70.2; H, 7.3; S, 8.75. $C_{21}H_{26}O_3S$ requires C, 70.35; H, 7.3; S, 8.95%).

(c) The acetate (22b) (155 mg, 0.49 mmol) was stirred at room temperature for 2 h in methanol (10 ml) and dichloromethane (5 ml) containing concentrated hydrochloric acid (1 ml) and then poured into cold aqueous sodium hydrogen carbonate. Extraction with dichloromethane followed by the work-up left a viscous syrupy residue which was purified by preparative t.l.c. [benzene–ethyl acetate (20 : 1) with triple development] to afford two fractions. The more-polar fraction gave recovered starting ketone (22b) (69.9 mg), m.p. 101—104 °C (ether–light petroleum). The less-polar fraction was found to be a mixture of $\Delta^8$- and $\Delta^{9(11)}$-*homoestratetraenes* (23e) and (24b) (97.2 mg, 89.5% based on the recovered starting material) which gave a crystalline mixture (85.9 mg; 1 : 2.6 by n.m.r.), m.p. 166—167 °C (ether). This material was again subjected to careful preparative t.l.c. (benzene with five times development), affording two fractions. The less-polar fraction (47.6 mg) gave a 1 : 1.3 mixture of both double-bond isomers (23e) and (24b) (31.8 mg), m.p. 167—168 °C. The more-polar fraction (28.6 mg), on two crystallizations from ether–dichloromethane, provided the *pure* $\Delta^{9(11)}$-*isomer* (24b) (20.1 mg), m.p. 174—176 °C, $\nu_{max.}$ 1 749, 1 723 (OAc), 1 606, 1 569, and 1 494 $cm^{-1}$ (styrene); $\lambda_{max.}$(EtOH) 263 nm (ε 18 600); δ($CDCl_3$) 0.96 (3 H, s, 13-Me), 2.07 (3 H, s, OAc), 3.78 (3 H, s, OMe), 4.88 (1 H, q, *J* 4.5 and 11 Hz, 17a-H), 6.03br (1 H, t, *J* 4.5 Hz, 11-H), and 6.5—7.6 (3 H, m, ArH); *m/e* 358 ($M^+$) (Found: C, 70.1; H, 7.3; S, 8.85. $C_{21}H_{26}O_3S$ requires C, 70.35; H, 7.3; S, 8.95%).

16-*Thia*-D-*homoestradiol* 3-*Methyl Ether* (25a) *and its Acetate* (25b).—A solution of a mixture of the tetraenes (23e) and (24b) (1.9 : 1 ratio by n.m.r.) (82.7 mg, 0.23 mmol) in dry tetrahydrofuran (5 ml) was added dropwise at −70 °C to a stirred solution of lithium (40.4 mg) in liquid ammonia (20 ml) containing freshly distilled aniline (2 ml). After 15 min, the reaction was quenched with ammonium chloride to discharge the blue colour and then the ammonia was allowed to evaporate. The residue was poured into water and extracted with ether–dichloromethane (3 : 1). Work-up left a crystalline product (79.8 mg) which was purified by preparative h.p.l.c. [n-hexane–ethyl acetate (7 : 1)], furnishing pure 3-*methoxy*-16-*thia*-D-*homoestradiol* (25a) (53.2 mg, 72.4%) as a crystalline solid, m.p. 128—131 °C (acetone–pentane), $\nu_{max.}$ (dilute $CCl_4$) 3 632 $cm^{-1}$ (free OH); δ($CDCl_3$) 0.88 (3 H, s, 13-Me), 3.76 (3 H, s, OMe), and 6.5—7.3 (3 H m, ArH); *m/e* 318 ($M^+$) (Found: C, 71.5; H, 8.3; S, 9.95. $C_{19}H_{26}O_2S$ requires C, 71.65; H, 8.25; S, 10.05%). The *acetate* (25b), prepared by the standard procedure, had m.p. 168—170 °C (dichloromethane–ether), $\nu_{max.}$($CHCl_3$) 1 740, 1 720 (OAc), 1 620, 1 575, and 1 502 $cm^{-1}$; δ($CDCl_3$) 0.95 (3 H, s, 13-Me), 2.04 (3 H, s, OAc), 3.74 (3 H, s, OMe), 4.84 (1 H, q, *J* 4.5 and 10.5 Hz, 17a-H), and 6.5—7.3 (3 H, m, ArH).

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