Synthesis of Aromatic Steroids by Palladium(0) Coupling and Electrocyclic Ring Closure

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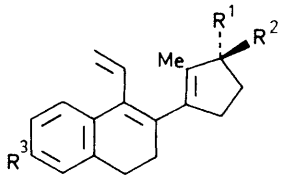
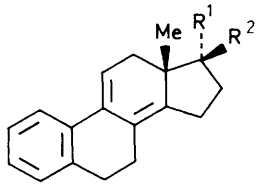
The naphthylcyclopentenone (**1a**) is reduced with sodium borohydride to the alcohol (**1c**). This cyclises when heated in xylene to give the estra-1,3,5(10),8(14),9(11)-pentaen-17-ols (**2**). The 17α-alcohol (**2a**) is the major component of the mixture and is isolated pure. When the cyclopentanol (**1c**) is heated in bromobenzene, the products are the estra-1,3,5(10),8,14-pentaen-17-ols (**3b**) and (**3c**), together with a hydrocarbon, the 17-methylcyclopenta[*a*]phenanthrene (**5a**). This compound is probably formed from the alcohols (**2**) or (**3**) by an acid-catalysed 1,2 methyl shift. The corresponding cyclopentenol (**1d**) has been prepared from the bromonaphthalene (**6**) and 3-(t-butyldimethylsilyloxy)-1-iodocylopentene (**7**) by palladium(0)-catalysed cross coupling. This cyclises in bromobenzene to give the cyclopentaphenanthrene (**5b**) and the alcohols (**3d**) and (**3e**). The known estrone intermediate (**9**) has been prepared by oxidation of these alcohols.

In the preceding paper we described a method for the construction of six-membered rings which involved the palladium(0)-catalysed cross coupling of monoene and diene units, followed by electrocyclisation of the resulting trienes.[1] Such a route seemed to offer a short method of preparation of some aromatic steroids, and indeed we had previously prepared some prototypes using an electrocyclic reaction to construct ring C.[2] This mode of formation of ring C is different from that used in any of the existing routes to steroids. It offers the possibility of producing derivatives with new substitution patterns, and it might allow unusual functional groups or heteroatoms to be incorporated, since electrocyclic reactions are known to be relatively insensitive to substituent effects.[3] In order to evaluate the method our first targets have been known steroids of the estrone family.

Our initial attempts to achieve such a synthesis were based on the ketone (**1a**). However, as described in the preceding paper, these attempts were thwarted because the ketone underwent a [1,7] hydrogen shift before the electrocyclisation took place. Since we had earlier shown that the dithioacetal (**1b**) could be cyclised successfully by heating in solution[2] it is clear that the nature of the functional group is important in determining the type of reaction which takes place. The carbonyl group of (**1a**) apparently promotes the [1,7] hydrogen shift, possibly by





(**1**) **a**; R^1R^2 = =O, R^3 = H
b; R^1R^2 = SCH_2CH_2S, R^3 = H
c; R^1 = OH, R^2 = R^3 = H
d; R^1 = OH, R^2 = H, R^3 = OMe
e; R^1 = $OSiMe_2Bu^t$, R^2 = H, R^3 = OMe

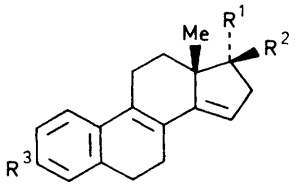
(**2**) **a**; R^1 = OH, R^2 = H
b; R^1 = H, R^2 = H

increasing the polarisation of the triene. There is little information in the literature on the effects of substituents on the rates of sigmatropic hydrogen shifts; one related observation is that [1,5] hydrogen shifts in dihydrotropones are faster, and have a lower enthalpy of activation, than in cycloheptadienes.[4] It therefore proved necessary to modify the precursor in order to achieve the desired cyclisation. Various attempts to protect the carbonyl group of compound (**1a**) were unsuccessful, and we decided to prepare the alcohols (**1c**) and (**1d**) as suitable materials for cyclisation.

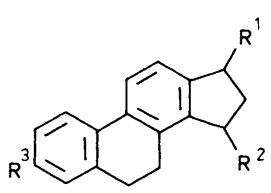
Two approaches were investigated. The first was based on the reduction of the ketone (**1a**) to the alcohol (**1c**). This was then cyclised by heating in xylene or bromobenzene. The second was based on the cross coupling of a protected iodocyclopentenol and the cyclisation of the resulting alcohol (**1d**).

Cyclisation of the Alcohol (**1c**).—Compound (**1c**) was prepared in good yield by reduction of the ketone (**1a**) with sodium borohydride. This was cyclised by heating in xylene until all the starting material had been consumed (32 h). The crude product contained two components which were tentatively identified as the isomeric pentaenols (**2a**) and (**2b**). These alcohols, and particularly the minor isomer (**2b**), were unstable in air and only the major isomer could be separated by flash column chromatography. This compound, which was isolated in 65% yield, was formulated as the 17α-alcohol (**2a**) on the basis of its ^{1}H n.m.r. spectrum. The position of the double bonds in compound (**2a**) is indicated by the signal for 11-H, which appears characteristically [2] as a double doublet (*J* 6.4 and 2.9 Hz) at δ 6.12. The assignment of the α-configuration at position 17 is based on comparison with literature models. In compound (**2a**) the signal for 17-H is a doublet (*J* 3.8 Hz) at δ 3.92. The n.m.r. of the 17α-acetate (**3a**) is reported to show 17-H as a doublet (*J* 5 Hz) at δ 5.15.[5] A comparison of the spectra of the α- and β-estratetraenols (**4a**) and (**4b**) shows that the signal for 17-H of the α-isomer occurs at higher field, and has smaller coupling constants.[6]

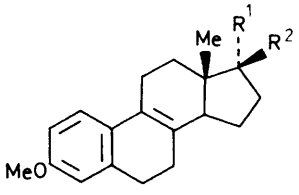
In order to shorten the reaction time, a cyclisation was also carried out in bromobenzene at reflux. The reaction was complete in 10 h but the product mixture contained three components, none of which was identical with either of the alcohols (**2**) obtained in the previous experiment. One of the products (39%) was a hydrocarbon, which was formulated as (**5a**) on the basis of its elemental analysis and spectra. The assignment of structure to this compound, and to the analogous compound (**5b**) which was isolated from a related experiment, is discussed separately below. The other two products were identified as the isomeric alcohols (**3b**) and (**3c**). These were initially isolated by chromatography as a 2:1 mixture. Further



(3) **a**; R^1 = OAc, R^2 = H, R^3 = OMe
b; R^1 = OH, R^2 = R^3 = H
c; R^1 = R^3 = H, R^2 = OH
d; R^1 = OH, R^2 = H, R^3 = OMe
e; R^1 = H, R^2 = OH, R^3 = OMe



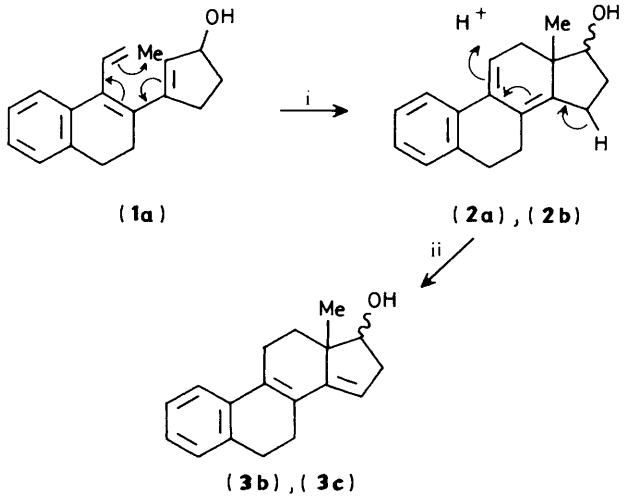
(5) **a**; R^1 = Me, R^2 = R^3 = H
b; R^1 = Me, R^2 = H, R^3 = OMe
c; R^1 = H, R^2 = Me, R^3 = OMe



(4) **a**; R^1 = OH, R^2 = H
b; R^1 = H, R^2 = OH

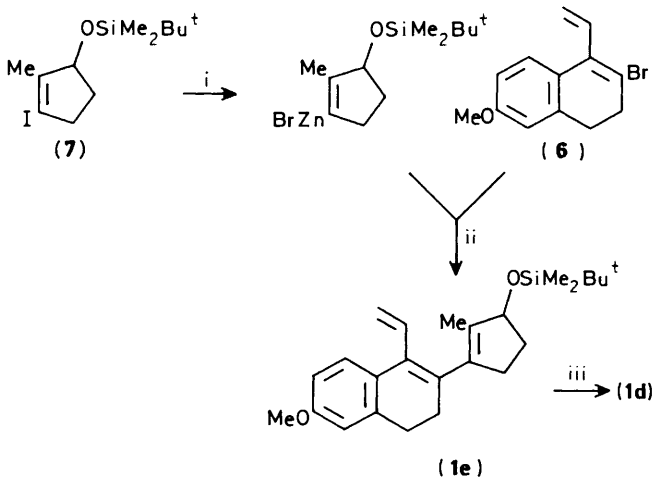
separation was attempted using medium pressure chromatography. This gave the alcohol (**3b**) (36%) as an oil; the isomer (**3c**) did not survive the chromatographic procedure. The major isomer (**3b**) was identified as the 17α-alcohol, and the minor isomer (**3c**) as the 17β-alcohol, on the basis of the 17-H signals in the n.m.r. spectra. The signal for (**3b**) appears as a broadened doublet (*J* 4.5 Hz) at δ 4.02, and that for (**3c**) is a double doublet (*J* 9.1 and 7.6 Hz) at δ 4.10.

As we observed in earlier work,[2] the 8(14),9(11)-diene system of compounds such as (**2**) is sensitive to traces of acid in the solvent, and it is likely that this is the cause of the formation of the alcohols (**3**) in this reaction. The overall sequence by which the alcohols are formed from the precursor (**1c**) is illustrated in Scheme 1.

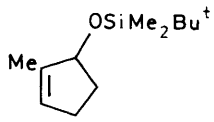


Scheme. 1. i, 139 °C; ii, H^+, 156 °C

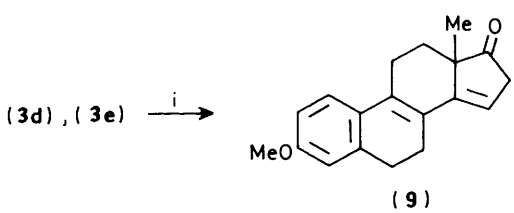
Formation and Cyclisation of the Alcohol (**1d**).—In the preceding paper we described a series of palladium(0)-catalysed cross coupling reactions with 2-bromo-1-vinylnaphthalene or its 6-methoxy derivative (**6**) as one of the components.[1] Coupling reactions of compound (**6**) were most efficiently achieved when it was used as the electrophile. As an extension of this type of process we constructed the silyl ether (**1e**) from the bromonaphthalene (**6**) and the protected iodocyclopentenol (**7**). Compound (**7**) was prepared in two steps from 3-iodo-2-methylcyclopent-2-enone. This compound was then treated in turn with t-butyl-lithium and zinc bromide. Addition of the bromonaphthalene (**6**) and a catalytic amount of $[Pd(PPh_3)_4]$ to a solution of this bromozinc intermediate led to the formation of the coupled silyl ether (**1e**), which was isolated (72%) as an oil. A by-product from the reaction was the silyl ether (**8**). The silyl ether (**1e**) was finally deprotected by heating with tetrabutylammonium fluoride to give the alcohol (**1d**) (Scheme 2).



Scheme 2. i, Bu^tLi, $ZnBr_2$; ii, $[Pd(PPh_3)_4]$; iii, $Bu_4N^+F^-$



The alcohol (**1d**) was heated in bromobenzene for 5 h with the intention of forming the alcohols (**3d**) and (**3e**), both of which are known compounds.[7] The mixture of products from the cyclisation was separated by flash chromatography into two fractions. The first of these consisted of a single substance which was identified as compound (**5b**). The second fraction consisted of a 1:1 mixture of the alcohols (**3d**) and (**3e**), the components being identified, as before, by the characteristic signals for 17-H in the n.m.r. spectra. Attempts to separate the alcohols were not successful, so the mixture was oxidised, using chromium trioxide on Celite, to the known ketone (**9**) (Scheme 3). The



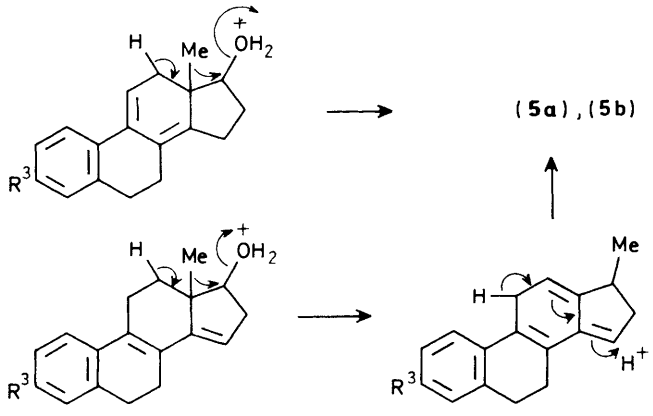
Scheme 3. i, CrO_3, Celite

physical properties and n.m.r. spectra of this ketone were in accord with those in the literature.[8]

Structure and Origin of Compounds (**5**).—Compounds (**5a**)

and (**5b**), which were found as significant products of the cyclisations carried out in bromobenzene, were characterised using u.v., ^{13}C n.m.r., ^{1}H n.m.r. [including 2D COSY spectra in the case of (**5b**)] and mass spectroscopy, and elemental analysis [for (**5a**)]. The ^{1}H n.m.r. spectrum of compound (**5b**) shows no vinylic signals but there is a new AB pattern in the aromatic region. The signal for the *C*-methyl group appears as a doublet (*J* 7.0 Hz) at δ 1.16. The ^{13}C n.m.r. shows signals for seven quaternary aromatic carbon atoms, five aromatic CH, one aliphatic CH, four CH_2, and two CH_3. The u.v. spectrum shows $\lambda_{max.}$ 280 nm, which is consistent with the presence of a dihydrophenanthrene nucleus. These data and the couplings revealed by the 2-D spectrum pointed to (**5b**) or its positional isomer (**5c**) as tenable structures. A search of the literature revealed that (**5b**) is a known compound, the reported m.p. and spectral data of which are in close agreement with those which we have obtained.[9] The data for compound (**5a**) are very similar and show that the structures of the two compounds are analogous.

A reasonable explanation for the formation of these compounds is that they result from dehydration of the starting alcohols, probably in an acid-catalysed process. The dehydrative 1,2-shift of a methyl group in 17-hydroxy steroids is a well established process.[10] It is likely, therefore, that the estrapentaenols (**2**) or (**3**) undergo this rearrangement when



Scheme 4.

heated in bromobenzene. Indeed we observed that if the reaction time of the cyclisation of compound (**1d**) in bromobenzene was prolonged, compound (**5b**) became the only detectable product. A probable reaction sequence is illustrated in Scheme 4.

One interesting question concerning the rearrangement is whether it shows any selectivity between 17α- and 17β-alcohols. Reactions of this type are known both in the 17α- and in the 17β-series.[11] The rearrangement would be expected to occur more rapidly with the 17α-alcohols since the hydroxy and methyl groups are much better arranged to allow concerted migration. Some tentative evidence for this is provided by the observation that as the proportion of compound (**5**) in the reaction mixtures increases, the ratio of 17α- to 17β-alcohols decreases. The initial electrocyclisation process shows good selectivity in favour of the α-alcohol.

In conclusion, we have succeeded in our preliminary aim of preparing some known steroidal compounds in the estrone family. The side-reactions which occur have been rationalised, and are probably capable of being circumvented. The method appears to be capable of further extension.

Experimental

For details of spectrometers and general methods see the preceding paper.

2-(1-*Hydroxy*-2-*methylcyclopent*-2-*en*-3-*yl*)-1-*vinyl*-3,4-*dihydronaphthalene* (**1c**).—The ketone (**1a**)[2] (100 mg, 0.39 mmol) was heated under reflux in ethanol (50 ml) with sodium borohydride (45 mg, 1.2 mmol) for 2 h. Water was added and the product was extracted into dichloromethane. The solution was dried and evaporated. Flash chromatography (silica) gave [with ether–petroleum (1:1)] the *alcohol* (85 mg, 86%) as an oil [Found: *m/z* 252 (M^+). $C_{18}H_{20}O$ requires *m/z* 252]; $\nu_{max.}$ 3 320 cm^{-1} (OH); δ(250 MHz) 1.52 (1 H, OH), 1.65 (3 H), 1.68—1.78 (2 H, m), 2.23—2.37 (4 H, m), 2.72 (2 H, t, *J* 7.2 Hz), 4.66 (1 H, d, *J* 5.7 Hz), 5.30 (2 H, dd, *AB*X), 6.41 (1 H, dd, AB*X*), 7.14—7.26 (3 H, m), and 7.50—7.54 (1 H, m): J_{AB} 1.8, J_{AX} 11.1, and J_{BX} 18.0 Hz); δ_C 13.53 (q), 28.56 (t), 29.07 (t), 33.37 (t), 33.76 (t), 81.73 (d), 117.48 (d), 126.29 (t), 126.72 (d), 127.22 (d), 128.04 (d), 132.31 (s), 136.46 (s), 136.68 (s), and 137.74 (s).

2-(1-*Hydroxycyclopent*-2-*en*-3-*yl*)-6-*methoxy*-1-*vinyl*-3,4-*dihydronaphthalene* (**1d**).—(a) 3-*Iodo*-2-*methylcyclopent*-2-*en*-1-*ol*. 3-Iodo-2-methylcyclopent-2-en-1-one[12] (2.0 g, 9.0 mmol) was heated in ethanol (80 ml) under reflux for 4 h with sodium borohydride (0.4 g, 10.9 mmol). Water was added and the product was extracted with dichloromethane. The solution was dried and evaporated and the residue was purified by flash chromatography, which gave [with ether–petroleum (1:1)] the *alcohol* (1.81 g, 89%), m.p. 82 °C (Found: C, 32.0; H, 4.0. C_6H_9IO requires C, 32.1: H, 4.0%); $\nu_{max.}$(film) 3 310 cm^{-1}; δ(250 MHz) 1.65 (1 H, OH), 1.70—1.81 (1 H, m), 1.83 (3 H), 2.32—2.45 (1 H, m), 2.58—2.63 (1 H, m), 2.73—2.85 (1 H, m), and 4.53 (1 H, br).

(b) *Silyl ether* (**7**). The alcohol (1.81 g, 8.08 mmol), imidazole (0.54 g, 8.8 mmol) and dimethyl-t-butylsilyl chloride (0.93 g, 8.8 mmol) were stirred in DMF (10 ml) under N_2 for 18 h. Water was added and the product was extracted by ether. The solution was dried and evaporated. The residue was purified by bulb-to-bulb distillation which gave the *silyl ether* (**7**) (2.1 g, 77%), b.p. 120 °C (bath) at 0.2 mmHg (Found: C, 43.1; H, 7.1. $C_{12}H_{23}IOSi$ requires C, 42.6; H, 6.85%); δ(250 MHz) 0.08 (6 H), 0.90 (9 H), 1.65—1.75 (1 H, m), 1.76 (3 H), 2.23—2.45 (2 H, m), 2.48—2.57 (1 H, m), 2.70—2.80 (1 H, m), and 4.57 (1 H, br).

(c) 2-(1-*Dimethyl*-t-*butylsilyloxy*-2-*methylcyclopent*-2-*en*-3-*yl*)-1-*vinyl*-3,4-*dihydronaphthalene* (**1e**). The freshly distilled silyl ether (**7**) (0.66 g, 2.0 mmol) in ether (20 ml) was cooled to −78 °C and t-butyl-lithium (4.2 mmol) was added. After 45 min the solution was warmed to −20 °C and zinc bromide (2.5 mmol) was added. The reaction mixture was stirred for 1 h. The bromonaphthalene (**6**)[2] (0.52 g, 2.0 mmol) and $[Pd(PPh_3)_4]$ (0.1 g, 4 mol%) were added in THF (15 ml) and the mixture was heated under reflux for 2.5 h. Flash chromatography gave the *silyl ether* (**1e**) (0.57 g, 72%) as an oil (Found: C, 75.7; H, 9.7. $C_{25}H_{36}O_2Si$ requires C, 75.7; H, 9.2%); δ(250 MHz) 0.10 (6 H), 0.90 (9 H), 1.62 (3 H), 1.70 (2 H), 2.40 (4 H), 2.72 (2 H. t), 3.80 (3 H), 4.66 (1 H, d), 5.26 (2 H, ddd, *AB*X), 6.39 (1 H, dd, AB*X*), 6.74 (2 H), and 7.40 (1 H, d). A second fraction was isolated and was identified as 1-*dimethyl*-t-*butylsilyloxy*-2-*methylcyclopent*-2-*ene* (**8**) (0.10 g, 23%), b.p. 70 °C (bath) at 0.2 mmHg (Found: C, 66.6; H, 11.4. $C_{12}H_{24}OSi$ requires C, 66.6; H, 11.2%); δ(250 MHz) 0.10 (6 H), 1.00 (9 H), 1.88 (3 H), 2.20—2.95 (6 H, m), 4.60—4.70 (1 H, m), and 5.61 (1 H, t).

(d) *Deprotection of the silyl ether*. Compound (**1e**) (0.50 g, 1.26 mmol) and tetrabutylammonium fluoride (1.5 mmol) in THF (30 ml) were heated under reflux for 10 min. Water was added and the product was extracted by dichloromethane. The solution was dried and evaporated to leave an oil. Flash chromatography gave [with ether–petroleum (1:1)] the *alcohol*

(**1d**) (0.31 g, 87%) as an oil (Found: C, 80.8; H, 8.2. $C_{19}H_{22}O_2$ requires C, 80.8; H, 7.8%); $\nu_{max.}$(film) 3 400 cm^{-1}; δ(250 MHz) 1.52 (3 H), 1.57—1.67 (1 H, m), 1.71 (1 H, OH), 2.11—2.30 (4 H, m), 2.40—2.47 (1 H, m), 2.58 (2 H, t), 3.70 (3 H), 4.56 (1 H, d, *J* 6.1 Hz), 5.18 (2 H, ddd, *AB*X), 6.30 (1 H, dd, AB*X*), 6.59—6.65 (2 H, m), and 7.35 (1 H, d); J_{AB} 1.8, J_{AX} 11.1, and J_{BX} 17.8 Hz); δ_C 12.76 (q), 27.81 (t), 28.82 (t), 32.67 (t), 33.05 (t), 55.18 (q), 80.99 (d), 110.70 (d), 113.40 (d), 116.42 (d), 122.72 (d), 127.22 (s), 131.22 (s), 133.44 (s), 133.94 (d), 135.80 (s), 138.83 (s), 140.01 (s), and 158.24 (s).

Cyclisation of the Alcohol (**1c**) *in Xylene.*—Compound (**1c**) (0.08 g, 0.32 mmol) was dissolved in dry degassed xylene (20 ml) and the solution was heated under reflux under N_2 for 32 h. The solvent was distilled off to leave an oil. Flash chromatography gave [with ether–petroleum (1:1)] *estra*-1,3,5(10),8(14),9(11)-*pentaen*-17α-*ol* (**2a**) (52 mg, 65%) as an oil (Found: *m/z* 252.1501. $C_{18}H_{20}O$ requires *m/z* 252.1514); $\nu_{max.}$(film) 3 340 cm^{-1}; δ(250 MHz) 0.91 (3 H), 1.88—1.91 (1 H, m), 1.98 (1 H, dd, *J* 18.2 and 6.6 Hz), 2.15 (1 H, OH), 2.13—2.22 (2 H, m), 2.35—2.55 (4 H, m), 2.72 (1 H, t, *J* 6.2 Hz), 2.92 (1 H, d, *J* 18.2 Hz), 3.92 (1 H, d, *J* 3.8 Hz), 6.12 (1 H, dd, *J* 6.4 and 2.9 Hz), 7.10—7.21 (3 H, m), and 7.56 (1 H, d).

Cyclisation of the Alcohol (**1c**) *in Bromobenzene.*—The alcohol (**1c**) (0.20 g, 0.8 mmol) was dissolved in bromobenzene (50 ml) and the solution was heated under reflux for 10 h. The solvent was evaporated off and the residue was subjected to flash chromatography. This gave [with ether–petroleum (1:1)] 17-*methyl*-7,15,16,17-*tetrahydro*-6H-*cyclopenta*[a]*phenanthrene* (**5a**) (40 mg, 39%) as an oil (Found: C, 91.9; H, 7.6. $C_{18}H_{20}$ requires C, 92.2; H, 7.75%); δ(250 MHz) 1.15 (3 H, d, *J* 6.9 Hz), 1.74—1.85 (1 H, m), 2.33—2.41 (1 H, m), 2.77—2.89 (5 H, m), 3.00—3.14 (1 H, m), 3.40 (1 H, t), 7.13—7.29 (4 H, m), 7.54 (1 H, d), and 7.76 (1 H, d); δ_C 20.67 (q), 25.80 (t), 29.62 (t), 31.58 (t), 34.26 (t), 38.76 (d), 123.11 (d), 123.37 (d), 124.43 (d), 127.41 (d), 127.54 (d), 128.57 (d), 133.39 (s), 133.55 (s), 137.51 (s), 137.73 (s), 143.45 (s), and 147.24 (s).

Further elution gave a mixture of estra-1,3,5(10),8,14-pentaen-17α-ol (**3b**) and the -17β-ol (**3c**) in a ratio of 2:1 by n.m.r.; δ(250 MHz) 0.93 (2 H), 1.67—1.76 (2 H, m), 1.94—2.06 (2 H, m), 2.36 (1 H, dd, *J* 18.3 and 3.3 Hz), 2.60—2.82 (4 H, m), 3.00 (1 H, d, br, *J* 18.3 Hz), 4.02 [0.66 H, d, *J* 4.5 Hz, 17-H of (**3b**)], 4.10 [0.33 H, dd, *J* 9.1 and 7.6 Hz, 17-H of (**3c**)], 5.56 (0.33 H, t, 15-H), 5.65 (0.66 H, t, 15-H), 7.12—7.35 (3 H, m), and 7.30—7.35 (1 H, m). The mixture was subjected to medium pressure chromatography, with chloroform as eluant. This gave the *alcohol* (**3b**) (30 mg, 36%) as an oil (Found: *m/z* 252.1510. $C_{18}H_{20}O$ requires *m/z* 252.1514); δ(250 MHz) 0.93 (3 H), 1.59 (1 H, OH), 1.65—1.74 (2 H, m), 1.94—2.07 (2 H, m), 2.34 (1 H, dd, *J* 18.2 and 3.3 Hz), 2.43—2.91 (4 H, m), 2.98 (1 H, d, br), 4.02 (1 H, d, *J* 4.5 Hz), 5.64 (1 H, s, br), and 7.12—7.35 (4 H, m). The minor isomer was unstable and could not be isolated pure.

Cyclisation of Alcohol (**1d**).—The alcohol (**1d**) (0.20 g, 0.7 mmol) was dissolved in bromobenzene (60 ml) and the solution was heated under reflux for 5 h. The solvent was evaporated off and the residue was subjected to flash chromatography. Ether–petroleum (1:1) gave 3-methoxy-17-methyl-7,15,16,17-tetrahydro-6*H*-cyclopenta[*a*]phenanthrene (**5b**) (90 mg, 48%), m.p. 81—82 °C (lit.,[9] m.p. 82—83 °C) (Found: *m/z* 264.1518. Calc. for $C_{19}H_{20}$: *m/z* 264.1514); $\lambda_{max.}$(MeCN) 280 nm; δ(250 MHz) 1.16 (3 H, d, *J* 7.0 Hz), 1.76—1.84 (1 H, m), 2.20—2.36 (1 H, m), 2.74—2.88 (5 H, m), 3.08—3.14 (1 H, m), 3.35—3.44 (1 H, m), 3.83 (3 H), 6.77—6.85 (2 H, m), 7.13 (1 H, d), 7.49 (1 H, m), and 7.63 (1 H, d); δ_C 20.60 (q), 25.76 (t), 29.95 (t), 31.46 (t), 34.23 (t), 38.68 (d), 55.76 (q), 112.83 (d), 113.95 (d), 122.37 (d), 123.27 (d), 125.56 (d), 128.66 (s), 132.54 (s), 133.23 (s), 138.98 (s), 142.40 (s), 147.14 (s), and 159.29 (2).

Further elution gave a mixture of 3-methoxyestra-1,3,5-(10),8,14-pentaen-17α-ol (**3d**) and the -17β-ol (**3e**) (100 mg, 50%) in a ratio of 1:1 by n.m.r. (Found: *m/z* 282.1611. Calc. for $C_{19}H_{22}O_2$: *m/z* 282.1620); $\nu_{max.}$(film) 3 380 cm^{-1}; δ(250 MHz) 0.92 (1.5 H), 0.96 (1.5 H), 1.66—1.72 (1 H, m), 1.82 (1 H, OH), 2.00 (1 H), 2.35 (1 H, dd, *J* 18.6 and 3.4 Hz), 2.55—2.69 (4 H, m), 2.71—2.79 (2 H, m), 3.00 (1 H, d, br), 3.80 (3 H), 3.99 [0.5 H, d, *J* 4.5 Hz, 17-H of (**3d**)], 4.05 [0.5 H, dd, *J* 9.1 and 7.6 H, 17-H of (**3e**)], 5.48 [0.5 H, t, *J* 2.4 Hz, 15-H of (**3e**)], 5.57 [0.5 H, t, *J* 2.4 Hz, 15-H of (**3d**)], 6.69—6.75 (2 H, m), and 7.25 (1 H, dd).

The cyclopenta[*a*]phenanthrene (**5b**) was the only detectable product of an analogous reaction carried out for 24 h.

3-*Methoxyestra*-1,3,5(10),8,14-*pentaen*-17-*one* (**9**).—The mixture of alcohols (**3d**) and (**3e**) (75 mg, 0.26 mmol) was dissolved in a mixture of ether (10 ml) and dichloromethane (30 ml). The solution was cooled to 0 °C and Celite (0.2 g) and chromium trioxide (75 mg, 76 mmol) were added. The mixture was stirred at 20 °C for 1.5 h after which the solids were filtered off and washed with ether. Flash chromatography gave (with chloroform) the ketone (**9**) (57 mg, 75%), m.p. 104 °C (lit.,[8] 101—104 °C); $\nu_{max.}$(Nujol) 1 740 cm^{-1}; δ(250 MHz) 1.17 (3 H), 1.53—1.65 (1 H, m), 2.06 (1 H, dt), 2.27—2.35 (1 H, m), 2.54—2.65 (3 H, m), 2.83 (2 H, t), 2.96 (1 H, dd, *J* 23.1 and 2.9 Hz), 3.34 (1 H, d, br, *J* 23.1 Hz), 3.83 (3 H), 5.88 (1 H, t, *J* 2.4 Hz), 6.73—6.77 (2 H, m), and 7.27 (1 H, d); δ_C 20.56 (q), 22.73 (t), 22.92 (t), 27.31 (t), 28.41 (t), 41.95 (t), 49.00 (s), 55.26 (q), 111.12 (d), 113.60 (d), 114.65 (d), 124.11 (s), 125.33 (s), 128.58 (s), 129.82 (s), 138.17 (s), 146.91 (s), 159.63 (s), and 220.00 (s).

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References

1 T. L. Gilchrist and R. J. Summersell, *J. Chem. Soc., Perkin Trans. 1*, preceding paper.
2 T. L. Gilchrist and J. E. Stanford, *J. Chem. Soc., Perkin Trans. 1*, 1987, 225.
3 E. N. Marvell, 'Thermal Electrocyclic Reactions,' Academic Press, New York, 1980; E. N. Marvell, C. Hilton, and M. Cleary, *J. Org. Chem.*, 1983, **48**, 4272.
4 A. P. ter Borg and H. Kloosterziel, *Recl. Trav. Chim.*, 1963, **82**, 1189; C. W. Spangler, *Chem. Rev.*, 1976, **76**, 187.
5 C. H. Kuo, D. Taub, and N. L. Wender, *J. Org. Chem.*, 1968, **33**, 3126.
6 B. Schönecker, D. Tresseli, G. Schubert, L. Kohout, and J. Fajhos, *Collect. Czech Chem. Commun.*, 1978, **43**, 2609; B. Schönecker, D. Tresselt, J. Draffehn, K. Ponsold, G. Engelhardt, D. Zeigen, G. Schneider, I. Weisz-Vincze, and G. Dombi, *J. Prakt. Chem.*, 1977, **319**, 419.
7 T. Asako, K. Hiraya, and T. Miki, *Chem. Pharm. Bull.*, 1973, **21**, 107 (α-alcohol); K. K. Koshoev, S. N. Amanchenko, A. V. Platonova, and I. V. Torgov, *Izv. Akad. Nauk SSSR*, 1963, 2058 (β-alcohol).
8 E. D. Sternberg and K. P. C. Vollhardt, *J. Org. Chem.*, 1984, **49**, 1574.
9 M. Kimura, M. Kawata, K. Akajima, K. Harita, and T. Miura, *Chem. Pharm. Bull.*, 1973, **21**, 1741.
10 A. Cohen, J. W. Cook, and C. L. Hewett, *J. Chem. Soc.*, 1935, 445; M. Kimura, K. Akiyama, and T. Miura, *Chem. Pharm. Bull.*, 1972, **20**, 2511; L. J. Chinn and K. W. Salamon, *J. Med. Chem.*, 1977, **20**, 229.
11 M. Kimura, M. Kawata, K. Akajima, K. Harita, and T. Miura, *Chem. Pharm. Bull.*, 1973, **21**, 1720.
12 R. H. Bradbury, T. L. Gilchrist, and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1981, 3234.

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