Polycyclic Analogues of *trans*-Decalones. Part 6.[1] Synthesis, Optical Resolution and Circular Dichroism of *trans-transoid-trans*-Perhydrophenanthren-1-one and *trans-transoid-trans*-Perhydrophenanthren-2-one

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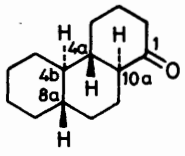
Racemic perhydrophenanthren-1-one and perhydrophenanthren-2-one have been synthesised from the tricyclic enone (±)-(3). The derived saturated equatorial hydroxy-compounds (8a) and (4a), resolved as their 3β-acetoxyandrost-5-ene-17β-carboxylates, afforded the (−)-(4a*S*,4b*R*,8a*S*,10a*S*)-perhydrophenanthren-1-one (1) and (−)-(4a*R*,4b*R*,8a*S*,10a*R*)-perhydrophenanthren-2-one (2), respectively, of high optical purity. C.d. measurements on both ketones have been made and the results are discussed.

A final summary of all the c.d. data now available (in both *ca.* 290 and *ca.* 190 nm, wavelength ranges) for a variety of unsubstituted 'all-*trans*' polycyclic ketones, belonging to the perhydro-anthracene, -naphthacene, and -phenanthrene series, is included, making possible comparisons with previous empirical estimates.

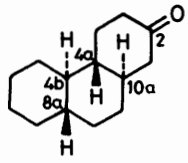
Five previous papers in this series [1–5] have been concerned with the study of the c.d. of some unsubstituted 'all-*trans*' ketones belonging to the perhydro-naphthalene,[2] -anthracene,[2,3] -naphthacene,[4] and -phenanthrene [1,5] structural types. Our aim was to provide reliable answers to specific questions concerning the contribution of key structural features to chiroptical properties of carbonyl compounds, which were put forward with the proposal of empirical rules by Kirk and Klyne.[6,7]

In this paper we report novel c.d. data for the hitherto unknown *trans-transoid-trans*-perhydrophenanthren-1-one (1), and for the *trans-transoid-trans*-perhydrophenanthren-2-one (2), previously described only in its racemic form. Being the final part of our study of the c.d. of extended 'all-*trans*'-decalones, we also present an overall summary of previous results and the conclusions reached about the c.d. properties of the aforementioned classes of ketones.



(1)

4a*S*, 4b*R*, 8a*S*, 10a*S*



(2)

4a*R*, 4b*R*, 8a*S*, 10a*R*

Results and Discussion

Synthesis and Optical Resolution.—The tricyclic enone (±)-(3) has been used as a common intermediate in the syntheses of the ketone (±)-(1) and of its already known [8] isomer (±)-(2). The preparation of (±)-(3) was by a novel and improved procedure which we have recently published.[9]

Reduction of (±)-(3) with lithium in liquid ammonia led to the ketone (±)-(2) or to its HO-*eq*-alcohol (±)-(4a), depending on experimental conditions. Thus, by using a large excess of lithium and methanol, the alcohol was isolated in very good yield (91%), while employing a stoicheiometric amount of metal and ammonium chloride led to the ketone in a 60% yield. On the other hand, chromic oxidation of (±)-(4a) quantitatively yielded (±)-(2).

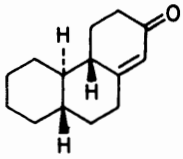
The ketone (±)-(1) was prepared in 40% overall yield from the enone (±)-(3) *via* the following sequence of reactions: epoxidation, rearrangement in an acidic medium, and reduction. This procedure is the same as that previously used in the syntheses of other isomeric tricyclic ketones [3,5] except for some minor modifications; it is noteworthy only in respect of the transformation of the mixture of α,β-epoxy-ketones (±)-(5) into the keto-enol (±)-(6).

Reaction of compound (±)-(3) with H_2O_2 under alkaline conditions, after an adaptation of the procedure of Wolff *et al.*[10] quantitatively led to a mixture of diastereoisomeric α,β-epoxy-ketones, one of them predominating as seen by t.l.c. analysis. No attempt was made to determine their relative configurations.

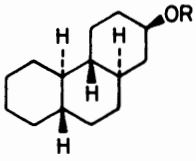
Conversion of the mixture of epoxy-ketones (±)-(5) into the keto-enol (±)-(6) was accomplished by using as acidic reagents H_2SO_4–AcOH, H_2SO_4–$EtCO_2H$, and $BF_3{\cdot}Et_2O$–benzene, with yields of 22, 65 and 55% respectively. H_2SO_4–AcOH was used under conditions identical with those previously described for other isomeric substrates,[3,5] but led to a mixture of compounds not fully identified † which only by a further acid treatment in aqueous acetone led to (±)-(6). This result, coupled with the low yield achieved in the desired compound, is in contrast with our previous experience for similar compounds already mentioned. Use of the reagent H_2SO_4–$EtCO_2H$ has been described before by Heusler *et al.*[11] for analogous transformations on steroidal substrates, though with some lower yields (52%). Reaction of the mixture of compounds (±)-(5) with $BF_3{\cdot}Et_2O$ in benzene was carried out after the procedure of Collins [12] for referenced compounds. In this case, in agreement with similar results obtained by that author, the lower homologous ketone (±)-(7) was isolated as a by-product (22%). This compound was characterized *via* formation of a 2,4-dinitrophenylhydrazone and by its spectral data.

The ketone (±)-(1) was finally obtained by reduction of the keto-enol (±)-(6) with refluxing HI–AcOH. Its m.p. (71—

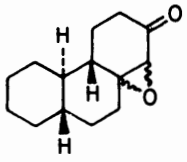
† Presumably products from the opening of the oxiran ring without subsequent elimination, *i.e.* dihydroxy-ketones and their *O*-acetyl derivatives.



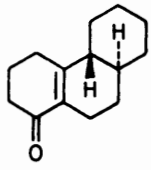
(3)



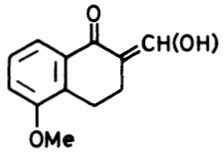
(4)
a; R = H
b; R = Ac



(5)



(10)



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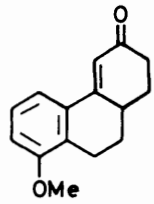

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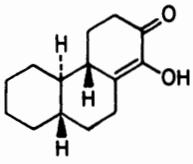

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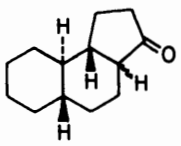
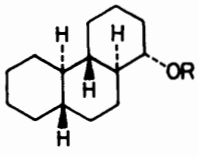
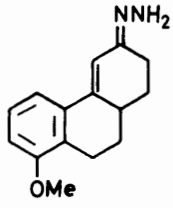


(7)



(8)
a; R = H
b; R = Ac



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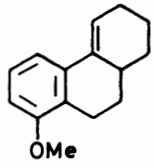

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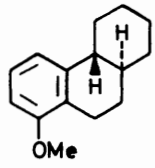

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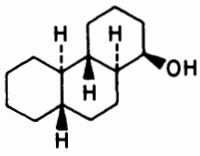


(9)

72 °C) as well as that of its semicarbazone (242—244 °C) are different from those cited in the literature [13] for a compound of connectivity identical with that (1) but of unspecified ring-junction stereochemistry. In our case, the relative configurations of three of the four stereogenic centres of the molecule are implied in the starting material for the synthesis, and the *trans* configuration for (C-10a), this centre being adjacent to the carbonyl group, is secured by the strongly acidic conditions used to obtain (±)-(1), which allow epimeric equilibration.

Reduction of (±)-(1) with $LiAlH_4$ gave a mixture of epimeric alcohols (±)-(8a) and (±)-(9), containing some 65% of the equatorial isomer, while reduction with lithium in liquid ammonia, after the procedure of Sondheimer *et al.*[14] for referable steroidal compounds led, in a practically quantitative yield, to the equatorial alcohol (±)-(8a), free of its axial epimer.

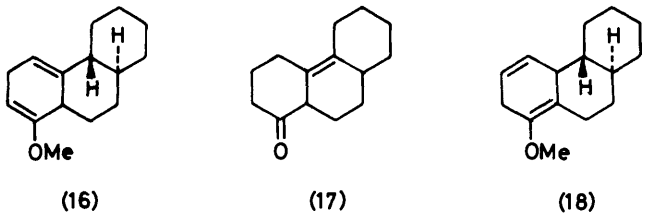
Although obtained in lower overall yield, compound (±)-(8a) was also synthesized by an independent method, namely, by reduction of the tricyclic enone (±)-(10) with Li/NH_3. Compound (±)-(10) was, in turn, prepared from 5-methoxy-1-tetralone, *via* an original synthetic route, which parallels that previously described by us [9] for the synthesis of (±)-(3). This procedure is simpler and results in better yields than those already described in the literature [15,16] for the preparation of the same compound (±)-(10).

5-Methoxy-1-tetralone was quantitatively transformed by ethyl formate and sodium hydride into the corresponding 2-hydroxymethylene derivative (11), which reacted with but-3-en-2-one in methanol using triethylamine as catalyst to give, after the final alkaline treatment, 1,9,10,10a-tetrahydro-8-methoxyphenanthren-3(2*H*)-one, (±)-(12). Reaction of the corresponding hydrazone (±)-(13) with potassium t-butoxide in refluxing toluene led to 1,2,3,9,10,10a-hexahydro-8-methoxyphenanthrene, (±)-(14). Reduction of this with an excess of lithium in liquid ammonia–THF followed by acidic hydrolysis (a standard procedure to obtain similar enones [9]) led to *trans*-1,2,3,4,4a,9,10,10a-octahydro-8-methoxyphenanthrene, (±)-(15), as the main product and only a small amount of the enone (±)-(10). This result is consistent with the known property of 1,2,3,4-tetrahydro-5-methoxynaphthalene systems being reduced with greater difficulty than the corresponding analogous 6-methoxy-derivatives.[17,18]

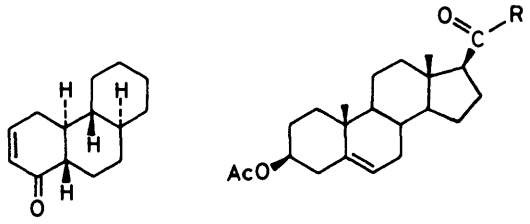
When a forced Birch reduction (after the modification of Johnson *et al.*[19]) was carried out on (±)-(14), with an excess of lithium in liquid ammonia–absolute ethanol, we obtained material from which a pure sample (t.l.c.) of the enol ether (±)-(16), identified as such by spectroscopic evidence (i.r. and n.m.r.), could be isolated. Protolysis of the crude material from this reduction gave the enone (±)-(10) as the main product in 38% overall yield. M.p.s of the 2,4-dinitrophenylhydrazone and semicarbazone of (±)-(10) agreed with those quoted in the literature [15] for the derivatives of the same compound synthesized by an independent method. Similar results were obtained for (±)-(15) upon reduction under identical forced conditions. In both cases, the β,γ-unsaturated enone (±)-(17), which was characterized on the basis of its 2,4-dinitrophenylhydrazone and spectral data, was formed as a minor by-product. Neither the other enol ether (±)-(18) which could have been produced in the reduction of (±)-(14) nor the α,β-unsaturated ketone (±)-(19) which would have resulted in the acidic hydrolysis of (±)-(18) and subsequent isomerization, could be detected in the reaction mixtures.

Optical resolutions were carried out by fractional crystallisation of the mixtures of diastereoisomeric esters obtained from 3β-acetoxyandrost-5-ene-17β-carbonyl chloride (20a) and the alcohols (±)-(4a) and (±)-(8a), which led to the less-soluble isomers of constant m.p. (21) and (22), respectively, Reductive cleavage of (21) by $LiAlH_4$ gave the (−)-alcohol (4a) which was oxidised to the (−)-ketone (2). Similarly, (+)-(8a) and (−)-(1) were obtained from (22). Absolute configurations shown in formulae for the resolved compounds were deduced from the sign of the ($n\rightarrow\pi^*$) Cotton effect of the ketones.

C.d. Properties.—Values of Δε now experimentally determined for (−)-(4a*S*,4b*R*,8a*S*,10a*S*)-perhydrophenanthren-1-one (1) and (−)-(4a*R*,4b*R*,8a*S*,10a*R*)-perhydrophenanthren-2-one (2) in three solvents of increasing polarity are given in the Table (entries 3 and 8), together with those already determined for the rest of the family of 'all-*trans*' extended decalones. Values previously predicted for all such structures

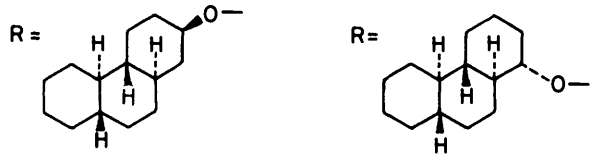


(16) (17) (18)



(19) (20)

a; R=Cl
b; R=OH



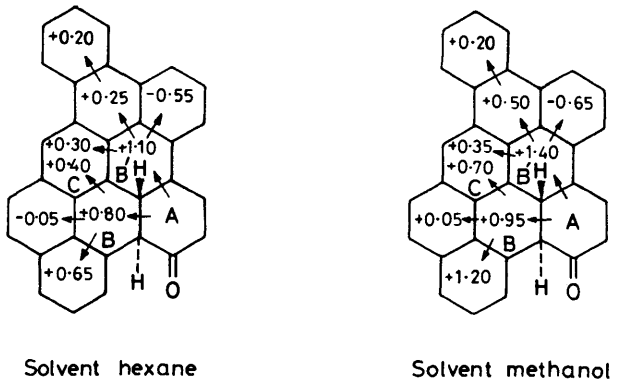
(21) (22)

on an empirical basis by Kirk and Klyne [6,7] are included for comparison.

Experimental values of c.d. for the ($n\rightarrow\pi^*$) transition of ketone (1) agree very precisely with those previously estimated by those authors from 19-nor-4-oxo-, D-homo-17a-oxo-, and 4-oxo-5α-steroids.[6] On the other hand, comparison of the actual c.d. values for (1) with those known for (4a*R*,8a*S*)-*trans*-1-decalone [6] (both sets smoothed to the nearest 0.05 unit) allow us to establish the contribution, δΔε, of the 'building of the third ring' as +0.40 (hexane) and +0.70 (MeOH) (see Figure 1 where are summarized all the conclusions of this kind which can be brought out from values of the Table). Differences between building a third ring C from an AB system or from an AB′, which Kirk and Klyne [6] had admitted to be relatively large, 0.45 (hexane) and 0.65 (MeOH) are, in fact, clearly smaller, 0.10 (hexane) and 0.40 (MeOH), thus confirming our previous suggestion.[1]

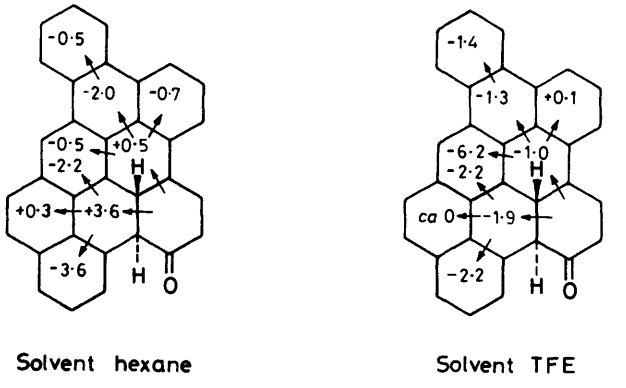
With regard to the same transition for ketone (2) (Table, entry 8), there appear marked differences between c.d. values now experimentally determined and those previously estimated in base to the chiroptical properties of des-A-5-oxo, 19-nor-3-oxo-, D-homo-17-oxo, and 3-oxo-5α-steroids.[6] Thus comparison of the values with the sign reversed for the enantiomer of (2) with those known for (4a*S*,8a*S*)-*trans*-2-decalone (Table and Figure 1) shows contribution of the third ring in (2) to Δε being fairly dissignate (*ca.* −0.5 to −0.6 units, depending upon solvent), while previous estimates rated it as negligible.[6]

Regarding c.d. values for the short wavelength transition *ca.* 190 nm it is worth noting that for ketone (1) (Table, entry 3), while Δε in TFE agrees perfectly with previous estimate, Δε in hexane, though being of the same sign of prediction, has an absolute value quite different. For ketone (2) (Table, entry 8) agreement between present experimental



Solvent hexane Solvent methanol

Figure 1. Observed c.d. contributions (δΔε) of each extra cyclohexane ring in 'all-*trans*' compounds of extended decalone type ($n\rightarrow\pi^*$ transition at *ca.* 290 nm). Arrows indicate connectivity of polycyclic systems; (+) sign indicates consignate behaviour; (−) indicates dissignate behaviour. The enantiomeric form of the compound, with sign of Δε reversed, was used for comparison where necessary



Solvent hexane Solvent TFE

Figure 2. Observed c.d. contributions (δΔε) of each extra cyclohexane ring in 'all-*trans*' compounds of extended decalone type (short wavelength transition at *ca.* 190 nm). Arrows indicate the manner of connection of rings where different values apply; (+) sign indicates consignate behaviour; (−) indicates dissignate behaviour. The enantiomeric form of the compound, with sign of Δε reversed, was used for comparison where necessary

values and those predicted is more satisfactory in hexane than in TFE. A summary of the contributions of each ring to Δε for this short wavelength transition taken from the experimental data for all our ketones, is presented in Figure 2.

Although neither of the tricyclic alcohols (4a) and (8a) present detectable c.d., it may be of interest as their enantiomers could be related to 4α-hydroxy-5α-steroids (with Δε of −0.38) [20] and to 3β-hydroxy-5α-steroids (with Δε between −0.23 and −0.56) [20] respectively. On the other hand, c.d. values found for their acetates [(4b), Δε *ca.* 0.0; (8b), Δε −0.60 (212 nm)] agree quite well with predictions made by Kirk *et al.*[21] (+0.1 and −0.60, respectively).

Summary of Our Previous Conclusions concerning C.d. Properties for 'All-trans' Extended Decalone Systems.—Here we summarize the main conclusions which can be deduced from a study of c.d. data for the more reliable $n\rightarrow\pi^*$ transitions, measured on our resolved 'all-*trans*' ketones and belonging to the tricyclic (perhydroanthracene and perhydrophenanthrene) and tetracyclic (perhydronaphthacene) systems. In each case data for the corresponding compound

Table. C.d. data for *trans*-decalones and their polycyclic analogues (wavelength in parentheses)

Entry no.	Compound	Solvent [a]	Δε(n→π*) Found	Δε(n→π*) Calc. [b]	Δε(Short wavelength) Found	Δε(Short wavelength) Calc. [c]
	trans-1-Decalone derivatives					
1	(−)-(4a*R*,8a*S*)-Perhydronaphthalen-1-one [d]	H	+0.81(296)	+0.8	+3.6(188)	+3.5
		M	+0.95(292)	+0.95		
		TFE			−1.9(189)	−2.0
2	(−)-(4a*S*,8a*R*,9a*S*,10a*R*)-Perhydroanthracen-1-one	H	+0.76(295)	+0.75	+3.9(187)	+3.8
		M	+1.01(290)	+1.0	<0(<196 [e])	
		TFE	+1.26(283)		−1.9(188)	−2.0
3	(−)-(4a*S*,4b*R*,8a*S*,10a*S*)-Perhydrophenanthren-1-one (1)	H	+1.20(296)	+1.2	+1.4(189)	+4.5
		M	+1.67(291)	+1.6	−2.1(192)	
		TFE	+2.16(285)		−4.1(190)	−4.0
4	(−)-(4a*R*,4b*R*,8a*S*,10a*S*)-Perhydrophenanthren-4-one	H	+1.46(295)	+1.45	≤0(195 [e])	?
		M	+2.14(293)	+1.95	−2.2(196 [e])	
		TFE	+2.34(288)		−4.1(195)	−5.0
	trans-2-Decalone derivatives					
5	(−)-(4a*R*,8a*R*)-Perhydronaphthalen-2-one [d]	H	−1.12(297)	−1.1	−0.5(190)	−0.5
		M	−1.37(290)	−1.4		
		TFE			+1.0(190)	+1.0
6	(−)-(4a*S*,8a*R*,9a*R*,10a*R*)-Perhydroanthracen-2-one [d]	H	−1.37(297)	−1.5	+1.5(185)	+1.0
		M	−1.86(290)	−1.9		
		TFE			+2.8(194)	+3.0
7	(−)-(4a*S*,5a*R*,6a*R*,10a*R*,11a*R*,12a*R*)-Perhydronaphthacen-2-one	H	−1.55(298)	−1.7	+2.0(187 [e])	+1.5
		M	−2.05(291)	−2.1	+1.4(198 [e])	
		TFE			+4.2(193)	+4.5
8	(−)-(4a*R*,4b*R*,8a*S*,10a*R*)-Perhydrophenanthren-2-one (2)	H	−0.56(297)	−1.1	+0.2(193)	0
		M	−0.72(288)	−1.4		
		TFE	−1.17(282)		+0.9(190)	+2.0
9	(+)-(4a*S*,4b*S*,8a*R*,10a*S*)-Perhydrophenanthren-3-one	H	+1.40(298)	+1.05	−1.0(195)	−0.5
		M	+1.70(290)	+1.35		
		TFE			−7.2(193)	−7.0
	' Middle-ring ' ketone					
10	(−)-(4a*S*,4b*R*,8a*S*,10a*R*)-Perhydrophenanthren-9-one	H	−0.47(296)	−0.3 [f]	−0.7 ± 0.4(190)	+3.0
		M	−0.75(293)	−0.4 [f]		

[a] H = n-hexane, M = methanol, TFE = 2,2,2-trifluoroethanol. [b] From ref. 6. [c] From ref. 7*c* and 7*d*. [d] From ref. 6; these Δε values are enclosed for comparison. [e] Limit of measurement. The exact wavelength of the c.d. maximum could not be determined from the experimental curves. [f] From simple additivity of the two *trans*-decalone systems (ref. 6); Δε values of −0.6 to −0.7 have previously been predicted by Kirk and Klyne.[6]

with one ring less has also been taken into account (see Table).

(−)-trans-cisoid-trans-cisoid-trans-*Perhydronaphthacen*-2-*one* [4] (*entry* 7). The fourth ring, which adds two bonds to the ' primary zig-zag ' of bonds, makes a small consignate contribution to Δε of *ca.* 0.2 units, both in methanol and in n-hexane (compare with entry 6).

(−)-trans-cisoid-trans-*Perhydroanthracen*-1-*one* [3] (*entry* 2). The third ring, which is in this case separate from the ' primary zig-zag ' of bonds, makes an almost negligible contribution to Δε (compare with entry 1).

(−)-trans-transoid-trans-*Perhydrophenanthren*-4-*one* [5] (*entry* 4): *front octant effects*. The third ' front octant ' ring makes a considerable contribution to Δε (consignate; 0.65—1.20 units, depending upon solvent polarity) (compare with entry 1).

(−)-trans-transoid-trans-*Perhydrophenanthren*-9-*one* [1] (*entry* 10). This represents the simplest ' middle-ring ' ketone in the ' all-*trans* ' perhydrophenanthrene class, and its c.d. data clearly prove that for such structures additivity of effects of the independent decalone systems fails to hold, the contribution of the 2-decalone fragment being the more important (compare with entries 1 and 5).

(−)-trans-transoid-trans-*Perhydrophenanthren*-3-*one* [1] (*entry* 9). The third ring makes a considerable consignate contribution to Δε (*ca.* 0.3 units) (comparison to be made with the enantiomer of that of entry 5). This result significantly differs from previous empirical predictions by Kirk and Klyne [6] (*ca.* 0.0). Further comparison with data for des-D-5α,-13β(*H*)-androstan-2-one shows that the consignate contribution of a β-axial methyl group in this case may be considerably smaller than that previously estimated [6] (0.1—0.2 units, instead of 0.45—0.60 units, depending upon solvent polarity).

Experimental

M.p.s were determined on a hot-plate and are uncorrected. Alumina was Merck grade I (Brockman); ' deactivated alumina ' refers to grade I with 2% of water. Silica gel was Merck Kieselgel 60 (70—230 mesh) grade II—III (Brockman). Unless otherwise stated, i.r. spectra were obtained for KBr discs and n.m.r. spectra for solutions in $DCCl_3$. Microanalyses were performed at Centro Nacional de Química Orgánica (C.S.I.C., Madrid). C.d. spectra were provided by Dr. P. M. Scopes and Prof. D. N. Kirk, Westfield College, London. In all cases organic extracts were combined, dried (Na_2SO_4), and evaporated under reduced pressure on a rotary evaporator. All optically resolved alcohols and ketones showed i.r. spectra

and g.l.c. behaviour identical with those of the corresponding racemates.

The tricyclic enone (±)-(3) was available from earlier work.[9]

(±)-trans-transoid-trans-*Perhydrophenanthren*-2eq-*ol*, rac-(4a).—A solution of the enone (±)-(3) (4 g) in THF (200 ml) was added to a stirred solution of lithium (3.8 g) in liquid ammonia (600 ml) and the mixture was stirred for a further 4 h. Anhydrous methanol (20 ml) was carefully added to consume the excess of Li and the ammonia was allowed to evaporate. After dilution with water and extraction with ether, the crude product (4.3 g) was crystallised from acetone, to give (±)-(4a) (2.85 g), m.p. 93—95 °C. A further crop (850 mg) was obtained by column chromatography of the residues (1.4 g) on silica gel [30 g; elution with benzene–ether (9 : 1)]. Total yield in the alcohol thus amounted to 91%. An analytical sample was obtained by recrystallisation from ethyl acetate, m.p. 94—95 °C; $\nu_{max.}$ 3 350, 1 055, and 1 045 cm^{-1}; δ 3.42 (1 H, $w_{h/2}$ 20 Hz, C*H*OH) (Found: C, 80.8; H, 11.4. Calc. for $C_{14}H_{24}O$: C, 80.7; H, 11.6%). Acetate, (±)-(4b), m.p. 50—51 °C; $\nu_{max.}$ 1 720, 1 260, and 1 215 cm^{-1}; δ 4.43 (1 H, $w_{h/2}$ 20 Hz, (C*H*OAc).

Previously, elution from the same chromatographic column with benzene had given the saturated ketone (±)-(2) (300 mg) as an oil (see spectral and analytical data below).

(±)-trans-transoid-trans-*Perhydrophenanthren*-2-*one*, rac-(2).—(*a*) The (±)-alcohol (4a) (100 mg) in acetic acid (18 ml) and water (1 ml) was oxidised with chromium(VI) oxide (60 mg) for 16 h at room temperature. The usual work-up, followed by chromatography on deactivated alumina (8 g; elution with benzene) gave the ketone (±)-(2) (90 mg) as an oil, which solidified at 0 °C (lit.,[8] 20.5—22 °C); $\nu_{max.}$ (liquid) 1 710 cm^{-1}; *m/z* 206 (M^+, 100) and 162 ($M^+ - 36$, 90%) (Found: C, 81.3; H, 10.70. Calc. for $C_{14}H_{22}O$: C, 81.5; H, 10.75%). 2,4-Dinitrophenylhydrazone, orange needles from acetone–ethanol, m.p. 195—196 °C (Found: C, 62.3; H, 6.55; N, 14.4. Calc. for $C_{20}H_{26}N_4O_4$: C, 62.2; H, 6.78; N, 14.49%).

(*b*) The enone (±)-(3) (1 g) in THF (30 ml) and anhydrous ether (30 ml) was reduced with lithium (slight excess over the stoicheiometrical amount) in liquid ammonia. The resulting blue solution was stirred for 1 h and the reaction mixture decomposed by ammonium chloride (3 g). Crude product (900 mg), isolated by use of ether, was a mixture containing the saturated ketone (±)-(2) and unchanged enone (±)-(3) in a ratio 60 : 40 (g.l.c.).

(±)-trans-transoid-1,10a-*Epoxyperhydrophenanthren*-2-*one*, rac-(5).—To a cooled (−5 °C) solution of the enone (±)-(3) (4.8 g) in methanol (450 ml) was added dropwise with stirring aqueous 4M-NaOH (16 ml) and then aqueous 30% H_2O_2 (60 ml). The reaction mixture was further stirred below 0 °C for 1 h before being poured into aqueous saturated NaCl (2 l). Extraction with ether and removal of the solvent afforded a colourless viscous oil (5.1 g) shown by t.l.c. to be a two-component mixture; $\nu_{max.}$ (liquid) 1 700, 865, and 845 cm^{-1}; δ 3.0 (1 H, s, O−CH). This mixture of crude epoxyketones was used without further purification.

(±)-trans-transoid-4,4a,4b,5,6,7,8,8a,9,10-*Decahydro*-1-*hydroxyphenanthren*-2(3H)-*one*, rac-(6).—(*a*) To a stirred solution of the above mixture of epoxyketones, (±)-(5) (4 g), in propanoic acid (40 ml) was added dropwise during 30 min a solution of concentrated H_2SO_4 (3.6 ml) in propanoic acid (8 ml). The resulting dark solution was kept at room temperature for 18 h and then diluted with water, cooled to 0 °C, and extracted with ether. The crude product (4.1 g) was recrystallised from methanol to give (±)-(6) (2.25 g), m.p. 123—125 °C. A further crop (350 mg) was obtained by chromatography of the residues on silica gel (20 g, elution with benzene). Total yield of (±)-(6) was 65%. An analytical sample was obtained by recrystallisation from acetone, m.p. 124—125 °C; $\nu_{max.}$ 3 400, 1 650, and 1 620 cm^{-1}; δ 6.1 (1 H, s, OH) (Found: C, 76.2; H, 9.32. Calc. for $C_{14}H_{20}O_2$: C, 76.3; H, 9.15%).

(*b*) To a stirred solution of (±)-(5) (1.38 g) in dry benzene (50 ml) under N_2 was added freshly distilled boron trifluoride–ether complex (0.8 ml); the mixture, which became greenish yellow, was then kept at room temperature for 19 h. After this it was diluted with ether (60 ml) and washed with 5% aqueous $NaHCO_3$ and water, and then dried and evaporated. The resulting yellowish viscous oil (1.4 g) was chromatographed on silica gel (40 g). Elution with benzene–ether (9 : 1) afforded first a colourless viscous oil (250 mg), pure by g.l.c., to which the structure (±)-(7) was assigned on the basis of its origin and of the following data: $\nu_{max.}$ 1 735 cm^{-1}; *m/z* 192 (M^+, 100). 2,4-Dinitrophenylhydrazone, yellow needles from methanol, m.p. 195—196 °C (Found: C, 61.5; H, 6.75; N, 15.3. Calc. for $C_{19}H_{24}N_4O_4$: C, 61.3; H, 6.45; N, 15.05%). Later fractions, eluted with the same solvent gave, after work-up, compound (±)-(6) (700 mg) as an oil which solidified with time.

(*c*) To a stirred solution of (±)-(5) (1 g) in acetic acid (12 ml) at 20 °C was added dropwise a solution of concentrated H_2SO_4 (1.3 ml) in acetic acid (7 ml). The resulting dark solution was stirred for 24 h and then diluted with water, cooled to 0 °C, and extracted with ether. The resulting crude oily product (900 mg), shown to be a mixture of compounds by t.l.c., was dissolved in acetone (20 ml), mixed with aqueous 30% H_2SO_4 (20 ml) and refluxed for 5 h. Work-up as before led finally to the purified compound (±)-(6) (220 mg).

(±)-trans-transoid-trans-*Perhydrophenanthren*-1-*one*, rac-(1).—A mixture of (±)-(6) (2.6 g), acetic acid (60 ml), and aqueous 57% HI (12 ml) was refluxed under N_2 for 90 min and then poured into a cold (0 °C) solution of NaOH (50 g) and $NaHSO_3$ (14 g) in water (300 ml). Extraction with ether and removal of the solvent afforded a crude oil (2.3 g) which was chromatographed on silica gel (40 g; elution with benzene) giving the racemic ketone (±)-(1) (1.5 g, 62%), as an oil which solidified with time. Crystallisation from n-hexane at −5 °C afforded the pure ketone (±)-(1), m.p. 71—72 °C; $\nu_{max.}$ 1 700 cm^{-1}; *m/z* 206 (M^+, 100), 163 (52), and 110 (52%) (Found: C, 81.7; H, 10.55. Calc. for $C_{14}H_{22}O$: C, 81.5; H, 10.74%). 2.4-Dinitrophenylhydrazone, orange needles from methanol, m.p. 232—233 °C (Found: C, 62.3; H, 6.55; N, 14.3. Calc. for $C_{20}H_{26}N_4O_4$: C, 62.2; H, 6.78; N, 14.49%). Semicarbazone, white needles from ethanol, m.p. 242—244 °C.

(±)-trans-transoid-trans-*Perhydrophenanthren*-leq-*ol*, rac-(8a).—(*a*) *From ketone* (±)-(1) *by reduction with lithium in liquid ammonia.* To a solution of the racemic ketone (±)-(1) (0.5 g) in THF (10 ml), liquid ammonia (100 ml) and anhydrous methanol (10 ml) was added lithium (0.5 g) in small pieces. The blue solution was stirred for 30 min and the reaction mixture decomposed by addition of ammonium chloride (5 g). The usual work-up, followed by extraction with ether, gave the equatorial alcohol (±)-(8a) (470 mg) (pure by g.l.c). Crystallisation from n-hexane afforded an analytical sample. of (±)-(8a), m.p. 117—118 °C; $\nu_{max.}$ 3 340, 1 055, 1 040, and 1 020 cm^{-1}; δ 3.1 (1 H, $w_{h/2}$ 20 Hz, C*H*OH) (Found: C, 80.9; H, 11.5. Calc. for $C_{14}H_{20}O$: C, 80.7; H, 11.6%). Acetate, (±)-(8b), m.p. 32—33 °C.

(*b*) *From the ketone* (±)-(1) *by reduction with* $LiAlH_4$ *in ether.* The racemic ketone (±)-(1) (150 mg) in dry ether (15 ml)

was refluxed for 2 h with $LiAlH_4$ (40 mg). Hydrolysis with cold dilute HCl and extraction with ether, gave the crude racemic alcohol (8a) containing some 35% (g.l.c.) of the axial-OH epimer (±)-(9). Chromatography of the crude product on silica gel (20 g) and elution with benzene–ether (95 : 5) gave first the axial alcohol (±)-(9) (50 mg) as an oil which solidified with time; m.p. 80—81 °C (n-hexane); $\nu_{max.}$ 3 380, 1 060, 992, and 970 cm^{-1}; δ 3.73 (1 H, $w_{h/2}$ 7 Hz, C*H*OH) (Found: C, 80.9; H, 11.3. Calc. for $C_{14}H_{24}O$: C, 80.7; H, 11.6%).

Later fractions, eluted with the same solvent afforded the equatorial alcohol (±)-(8a) (80 mg), m.p. 116—118 °C.

(*c*) *From the enone* (±)-(10) *by reduction with lithium in liquid ammonia.* The procedure was identical with that described above to prepare the alcohol (±)-(4a) from the enone (±)-(3). The enone (±)-(10) (1.4 g) (see preparation below) in THF (70 ml) was reduced with lithium (1.5 g) in liquid ammonia (250 ml) and THF (50 ml). Methanol (12 ml) was added to destroy excess of Li. Conventional work-up afforded a crude oil (1.24 g) which solidified with time. G.l.c. showed the presence of at least three components, all alcohols as indicated by the i.r. and n.m.r. spectra of the mixture, the major product being the alcohol (±)-(8a). Fractional recrystallisation of the crude product from n-hexane gave the pure alcohol (±)-(8a) (250 mg), m.p. 117—118 °C. Minor by-products could not be isolated.

Preparation of (±)-trans-3,4,4b,5,6,7,8,8a,9,10-*Decahydrophenanthren*-1(2H)-*one*, rac-(10).—2-*Hydroxymethylene*-5-*methoxy*-1-*tetralone*, (11). To a cooled and stirred suspension of NaH (50—60%) (7.2 g) in dry benzene (60 ml) under N_2 was added ethyl formate (16 ml) followed 15 min later by a solution of 5-methoxy-1-tetralone (10 g) in benzene (100 ml); the mixture was then stirred overnight. Ice-cold water was added to the mixture to dissolve the precipitated sodium salt and the benzene layer extracted thrice with aqueous 3% KOH. Combined alkaline extracts, after being washed with ether, were acidified with cold dilute HCl and the mixture extracted with ether–benzene. Removal of the solvent afforded a crude product (10.7 g), as a brown solid, which was used for the synthesis without further purification. Recrystallisation from aqueous methanol furnished an analytical sample with m.p. 68—69 °C; $\nu_{max.}$ 1 635 and 1 595 cm^{-1}; δ 3.8 (3 H, s, OCH_3), 8.1 (1 H, s, =C*H*OH) and 14.4 (1 H, $w_{h/2}$ 16 Hz, OH) (Found: C, 70.8; H, 6.15. Calc. for $C_{12}H_{12}O_3$: C, 70.6; H, 5.92%).

(±)-1,9,10,10a-*Tetrahydro*-8-*methoxyphenanthren*-3(2H)-*one*, rac-(12).—To a cooled (0 °C) and stirred solution of the hydroxymethylene derivative (11) (24 g) in anhydrous methanol (600 ml) under N_2 were added successively and rapidly triethylamine (33 ml) and freshly distilled but-3-en-2-one (11.7 ml) in methanol (50 ml). The reddish reaction mixture was left under N_2 at room temperature for 4 days and then made just acid with aqueous 30% acetic acid; it was then mixed with a solution of KOH (140 g) in water (175 ml) and refluxed under N_2 for 5 h. Most of the methanol, was removed from the mixture and the residue was diluted with water and extracted with benzene to afford a crude product (28.8 g); this was recrystallised from ethyl acetate to give (±)-(12) (16.3 g), as a pale yellow solid, m.p. 115—116 °C. An additional crop (1.95 g) of compound (±)-(12) was obtained by column chromatography of the residues (8.1 g) on silica gel [200 g; elution with benzene–ether (8 : 2)]. Total yield in (±)-(12) was then 65%; $\nu_{max.}$ 1 650 cm^{-1}; δ 3.8 (3 H, s, OCH_3), 6.6 (1 H, s, CH=C) (Found: C, 79.0; H, 6.90. Calc. for $C_{15}H_{16}O_2$: C, 78.9; H, 7.06%).

(±)-1,9,10,10a-*Tetrahydro*-8-*methoxyphenanthren*-3(2H)-*one Hydrazone*, rac-(13).—The methoxy enone (±)-(12) (10 g) in ethanol (150 ml), triethylamine (40 ml), and aqueous 80% hydrazine (70 ml) were refluxed for 90 min. Upon cooling and dilution of the mixture with water (±)-(13) separated as a yellow solid (9.3 g, 88%), m.p. 131—132 °C; $\nu_{max.}$ 3 340, 3 310, and 1 635 cm^{-1}; δ 3.8 (3 H, s, OCH_3), 5.1 (2 H, $w_{h/2}$ 16 Hz, NH_2), and 6.6—7.5 (4 H, m, olefinic and aromatic protons) (Found: C, 74.2; H, 7.7; N, 11.5. Calc. for $C_{15}H_{18}N_2O$: C, 74.4; H, 7.44; N, 11.6%).

(±)-1,2,3,9,10,10a-*Hexahydro*-8-*methoxyphenanthrene*, rac-(14).—A mixture of the hydrazone (±)-(13) (9 g), dry toluene (350 ml), and potassium t-butoxide (9.5 g) was refluxed for 24 h, and then added to aqueous 10% HCl (400 ml). The toluene layer was separated and the aqueous solution was extracted with ether. Work-up of the combined organic layers gave a reddish oil (8.5 g), which was chromatographed on deactivated alumina (180 g; elution with benzene) to yield (±)-(14), as a colourless viscous oil (6.5 g, 82%); $\nu_{max.}$ (liquid) 1 575 and 1 260 cm^{-1}; δ 3.77 (3 H, s, OCH_3), 6.4—7.3 (4 H, m, olefinic and aromatic protons) (Found: C, 84.3; H, 8.55. Calc. for $C_{15}H_{18}O$: C, 84.1; H, 8.41%).

Reduction of (±)-1,2,3,9,10,10a-*Hexahydro*-8-*methoxyphenanthrene*, rac-(14).—(*a*) *With lithium–ammonia–THF.* To a solution of lithium (4 g) in liquid ammonia (250 ml) and THF (120 ml) was added dropwise while stirring (±)-(14) (2 g) in THF (130 ml). After being stirred for 2 h, the reaction mixture was decomposed by the addition of methanol (50 ml), and the crude product (2 g) isolated by use of ether. The residue was dissolved in methanol (60 ml) and refluxed with aqueous 3M-HCl for 30 min. Partial removal of the methanol precipitated a solid which was filtered off, washed with cold methanol, and dried *in vacuo* to give compound (±)-(15) as white needles (1.1 g), m.p. 78—79 °C (methanol); $\nu_{max.}$ 1 580, 1 260, 1 250, and 1 085 cm^{-1}; δ 3.87 (3 H, s, OCH_3) and 6.6—7.3 (3 H, aromatic protons); *m/z* 216 (M^+, 100) (Found: C, 83.1; H, 9.45. Calc. for $C_{15}H_{20}O$: C, 83.3; H, 9.26%).

The above filtrate was diluted with water and extracted with ether to afford an oily residue (0.5 g) which was chromatographed on silica gel (15 g). Elution with benzene–ether (9 : 1) gave first an additional crop of (±)-(15) (100 mg). Later fractions, eluted with the same solvent, left a residue of 300 mg (crude), as a pale yellow oil, to which the structure of the enone (±)-(10) was assigned (see data below).

(*b*) *With lithium–ammonia–ethanol.* To a vigorously stirred solution of (±)-(14) (1.6 g) in anhydrous ethanol (600 ml) and liquid ammonia (1 400 ml), was added lithium (30 g) in small pieces during a 2 h period. During the second hour a further portion of ethanol (200 ml) was added. Once all the lithium had reacted, the ammonia was left to evaporate, water and ether were added, and the aqueous layer was extracted with ether. Conventional work-up afforded a crude oily residue (1.3 g), a portion of which (200 mg) was chromatographed on silica gel (15 g). Elution with benzene gave a product, to which the structure of the enol ether (±)-(16) was assigned; $\nu_{max.}$ (liquid) 1 690 and 1 660 cm^{-1}; δ 3.43 (3 H, s, OCH_3), 4.43 (1 H, t, *J* 4 Hz, 7-H), and 5.47 (1 H, m, 5-H).

The remainder of the crude residue (1.1 g) in methanol (70 ml) was mixed with concentrated HCl (1.5 ml) and water (10 ml), and refluxed for 1 h. The usual work-up (extraction with ether) gave a yellow oily product (900 mg), which was chromatographed on silica gel (25 g). Fractions eluted with benzene–ether (95 : 5) left an oily residue (50 mg) which solidified with time; m.p. 71—72 °C (n-hexane). For this compound the structure of the β,γ-unsaturated enone (±)-(17) was assigned on the basis of its origin and the following data: $\nu_{max.}$ 1 695 and 1 625 cm^{-1}; no u.v. maximum near 240 nm; no olefinic protons (n.m.r.). 2,4-Dinitrophenylhydrazone, yellow

needles from methanol, m.p. 237—239 °C (Found: C, 62.3; H, 6.5; N, 14.7. Calc. for $C_{20}H_{24}N_4O_4$: C, 62.5; H, 6.25; N, 14.7%).

Later fractions, eluted with benzene–ether (9 : 1), afforded the α,β-unsaturated enone (±)-(10) (450 mg, 38%) as a colourless oil (pure by g.l.c.); $\nu_{max.}$ 1 665 and 1 620 cm^{-1}; no olefinic protons (n.m.r.). 2,4-Dinitrophenylhydrazone, red needles from ethanol, m.p. 215—216 °C (lit.,[15] 215—216 °C). Semicarbazone, colourless needles from methanol, m.p. 225—226 °C (lit.,[15] 225 °C).

Reduction of (±)-(15) *with Lithium–Ammonia–Ethanol.*—Compound (±)-(15) (1.38 g) in anhydrous ethanol (500 ml) and liquid ammonia (900 ml) was reduced with lithium (19 g) as described before for compound (±)-(14). Final hydrolysis was achieved by refluxing the residue first obtained (960 mg) in methanol (100 ml) for 90 min. Chromatography of the resulting crude product as above, gave the enone (±)-(10) (470 mg, 36%) and the enone (±)-(17) (70 mg, 5%).

3β-*Acetoxyandrost-5-ene-*17β-*carboxylate* (21) *of the Tricyclic Alcohol* (4a).—A crude mixture of the diastereoisomeric esters was obtained from 3β-acetoxyandrost-5-ene-17β-carboxylic acid [22] (20b) (9.5 g), *via* its acid chloride (20a) in pyridine (60 ml) and the equatorial alcohol (±)-(4a) (4 g) in pyridine (80 ml), by the usual method [2] (extraction with ether). Chromatography on silica gel (200 g; elution with benzene) afforded the pure esters as a mixture (7.1 g) of both diastereoisomers inseparable on silica gel. This material was successively crystallised three times from ethyl acetate and then five times from acetone to give the ester (21) (370 mg). The two final crystallisations did not change the m.p. of the product, m.p. 165—166 °C (Found: C, 78.3; H, 10.05. Calc. for $C_{36}H_{54}O_4$: C, 78.5; H, 9.88%).

(−)-(2R,4aR,4bR,8aS,10aR)-*Perhydrophenanthren-*2-*ol* (4a).—The foregoing pure ester * (21) (350 mg) was reductively cleaved with $LiAlH_4$ (330 mg) in dry ether (60 ml) under reflux for 9 h. Hydrolysis with cold dilute HCl, extraction with ether, and removal of the solvent gave a mixture of the alcohol (4a) and 21-norpregn-5-ene-3β,20-diol, which was chromatographed on deactivated alumina (20 g). Elution with benzene–ether (9 : 1) gave the (−)-alcohol (4a) (120 mg), m.p. 116—117 °C (recrystallised from acetone); $[\alpha]_D^{23}$ −27° (*c*, 0.2 in $CHCl_3$). Acetate (4b), m.p. 56—58 °C (after sublimation at 80 °C and 18 mmHg); $[\alpha]_D^{23}$ −10° (*c*, 0.15 in $CHCl_3$).

(−)-(4aR,4bR,8aS,10aR)-*Perhydrophenanthren-*2-*one*, (2).—The (−)-alcohol (4a) (95 mg) was oxidised in acetic acid (15 ml) with chromium(VI) oxide (55 mg) for 4 h at room temperature. Work-up, followed by chromatography on deactivated alumina (7 g; elution with benzene) gave the (−)-ketone (2) (90 mg), as an oil; $[\alpha]_D^{23}$ −10° (*c*, 1.1 in $CHCl_3$).

3β-*Acetoxyandrost-5-ene-*17β-*carboxylate* (22) *of the Tricyclic Alcohol* (8a).—The acid chloride (20a), prepared from the steroidal acid (20b) (4.1 g), in pyridine (30 ml) was mixed with a solution of the tricyclic alcohol (±)-(8a) (1.6 g) in pyridine (30 ml) and refluxed for 2 days. Work-up (extraction with ether), gave a dark thick mass (6 g), chromatography of which on silica gel (80 g; elution with benzene) afforded the pure esters, as a mixture (2.9 g) of both diastereoisomers, inseparable on silica gel. This material was crystallised eight times from acetone to give the ester (22) (160 mg). The two final crystallisations did not change the m.p. of the product, 187—188 °C (Found: C, 78.4; H, 9.7. Calc. for $C_{36}H_{54}O_4$: C, 78.5; H, 9.88%).

(+)-(1S,4aS,4bR,8aS,10aS)-*Perhydrophenanthren-*1-*ol* (8a).—The pure ester * (22) (160 mg) was reductively cleaved with $LiAlH_4$ (150 mg) in dry ether (50 ml) under reflux for 6 h. Work-up gave a mixture (150 mg) of the alcohol (8a) and 21-norpregn-5-ene-3β,20-diol, which was chromatographed on deactivated alumina (15 g). Elution with benzene and benzene–ether (95 : 5) afforded the (+)-alcohol (8a) (60 mg), m.p. 145—146 °C after sublimation (90 °C at 18 mmHg), $[\alpha]_D^{23}$ +5° (*c*, 0.2 in $CHCl_3$). Acetate (8b), m.p. 53—54 °C, $[\alpha]_D^{23}$ +3.5° (*c*, 0.12 in $CHCl_3$), Δε, −0.6 (212 nm, in MeOH).

(−)-(4aS,4bR,8aS,10aS)-*Perhydrophenanthren-*1-*one* (1).—The (+)-alcohol (8a) (35 mg) in acetic acid (7 ml) was oxidised with chromium(VI) oxide (50 mg) for 4 h at room temperature. Work-up and percolation in benzene through deactivated alumina (5 g) gave the (−)-ketone (1) (33 mg), m.p. 83—84 °C after sublimation (80 °C at 18 mmHg); $[\alpha]_D^{23}$ −28° (*c*, 0.1 in $CHCl_3$).

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* Optical purity of all present products rests upon the criterion of constancy of m.p. of the 3β-acetoxyandrostenecarboxylate esters, which have given good results in other cases (refs. 1—5). Neither $[\alpha]_D$ nor the ^1H n.m.r. spectra of mixtures of diastereoisomeric esters varied significantly, whilst the m.p. asymptotically approached the value of that of the pure ester.

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