Optical Rotatory Dispersion and Circular Dichroism. Part LXXXI.[1] Optical Resolution of *trans*-1*eq*-Decalol, *trans*-2*eq*-Decalol, and *trans*,-*syn*,*trans*-Perhydroanthracen-2*eq*-ol

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The *trans*-decalols named in the title have been resolved by fractional crystallisation of their 3β-acetoxyandrost-5-ene-17β-carboxylates, and converted into *trans*-decalones of high optical purity. The enamine of (±)-*trans*-2-decalone condensed with but-3-en-2-one to give, after cyclisation, the enone (11) of the perhydroanthracene series. The derived saturated alcohol (14), resolved as its 3β-acetoxyandrost-5-ene-17β-carboxylate (13), afforded the perhydroanthracen-2-one (3).

OPTICALLY pure samples of *trans*-1-decalone (1), *trans*-2-decalone (2), and *trans*,*syn*,*trans*-perhydroanthracen-2-one (3) were required in connection with our investigations into the c.d. of ketones.[2] O.r.d. data for the $n \longrightarrow \pi^*$ transition were reported some years ago for *trans*-1-decalone [3,4] and *trans*-2-decalone,[4] but we needed reliable c.d. data in a series of solvents for both the $n \longrightarrow \pi^*$ and the $n \longrightarrow \sigma^*$ transitions.[5] The hitherto unknown tricyclic ketone (3) was needed for the same purpose.

Fractional crystallisation of esters of 3β-acetoxyandrost-5-ene-17β-carboxylic acid (4) is a convenient method for the optical resolution of chiral alcohols,[6] including *cis*,*cis*-1-decalol,[6b] and has proved satisfactory in the present cases.

trans-2eq-*Decalol*.—Commercial ' decahydro-2-naphthol ' [Aldrich; *ca.* 70% (±) *cis*-2-decalols] was isomerised over Raney nickel, as reported recently for the

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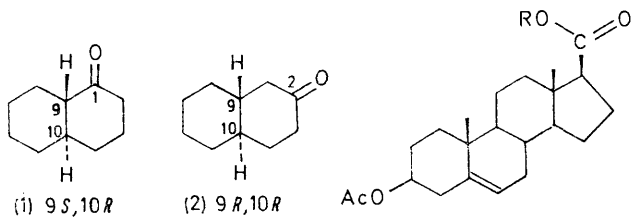
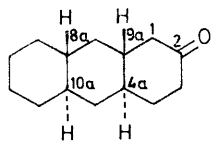
[1] Part LXXX, D. N. Kirk and R. J. Mullins, preceding paper.
[2] D. N. Kirk and W. Klyne, in preparation.
[3] C. Djerassi and W. Klyne, *J. Chem. Soc.*, 1962, 4929.
[4] W. Klyne, *Experientia*, 1964, **20**, 349.
[5] D. N. Kirk, W. Klyne, W. P. Mose, and E. Otto, *Chem. Comm.*, 1972, 35.
[6] (*a*) R. B. Woodward and T. J. Katz, *Tetrahedron*, 1959, **5**, 70; (*b*) C. Djerassi and J. Staunton, *J. Amer. Chem. Soc.*, 1961, **83**, 736; (*c*) C. Djerassi, E. J. Warawa, R. E. Wolff, and E. J. Eisenbraun, *J. Org. Chem.*, 1960, **25**, 917.

isomerisation of 5β- to 5α-steroids.[7] G.l.c. analysis showed the major products to be (±)-*trans*-2*eq*-decalol (5) (racemic), (±)-*trans*-2-decalone (2) (racemic), and

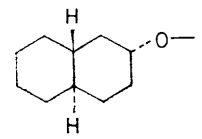


(1) 9*S*,10*R* (2) 9*R*,10*R*

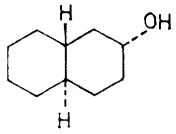
(4) R = H



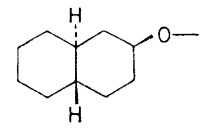
(3) 4a*S*, 8a*R*, 9a*R*, 10a*R*



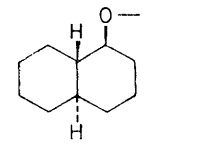
(6) R = H



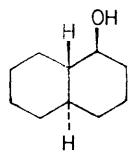
(5) 2*R*, 9*R*,10*R*



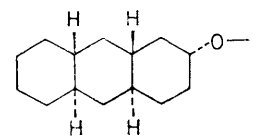
(7) R =



(9) R =



(8) 1*S*, 9*S*, 10*R*



(13) R =

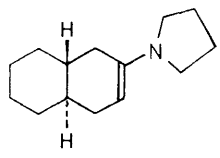
naphthalene; the proportion of naphthalene increased with time. The racemic decalol could be separated directly by chromatography on alumina, or in improved yield by first reducing the ketone in the mixture with lithium aluminium hydride.

The (±)-*trans*-2*eq*-decalol was converted into its 3β-acetoxyandrost-5-ene-17β-carboxylate in the usual way. Repeated fractional crystallisation from ethanol to constant m.p. achieved separation of the diastereoisomeric esters (6) and (7); these were reduced with lithium aluminium hydride to liberate the corresponding decalols, (5) and its enantiomer, which were of identical optical purity as estimated from D-line rotations (see Experimental section).

Oxidation of the more plentiful (+)-*trans*-2*eq*-decalol (5) gave (−)-*trans*-2-decalone, shown from the negative sign of its Cotton effect ($n \longrightarrow \pi^*$) to have the (9*R*)-configuration (2). The previously reported[4] o.r.d. amplitude *a* for the (9*S*)-enantiomer was +54 units (in methanol): the present sample had Δε −1·37, equivalent to a calculated *a* value of −55 units, by application of the expression $a = 40{\cdot}28\Delta\varepsilon$.[8]

trans-1eq-*Decalol*.—Commercial (±)-1-decalone (*cis*–*trans* ratio *ca.* 2 : 1 by g.l.c.) was equilibrated in acidified methanol, then reduced with sodium borohydride, to give a mixture rich in (+)-*trans*-1*eq*-decalol (8) (racemic), which was purified by crystallisation. The derived ester of 3β-acetoxyandrost-5-ene-17β-carboxylic acid afforded one diastereoisomer (9) in pure form after repeated fractional crystallisation. Reduction of this ester with lithium aluminium hydride gave (+)-(1*S*,9*S*)-decalol (8), which afforded (−)-*trans*-1-decalone (1) on oxidation; the positive Cotton effect ($n \longrightarrow \pi^*$) showed this ketone to have the (9*S*)-configuration illustrated. [Δε +0·95 in methanol; *a* (calc.)[8] +38; reported *a* value −40,[3,4] or −46,[9] for (9*R*)-*trans*-1-decalone].

trans,syn,trans-*Perhydroanthracen-2-one* (3).—(±)-*trans*-2-Decalone was converted into its pyrrolidine enamine derivative (10), which reacted with but-3-en-2-one, followed by acid, to give the tricyclic enone (11). This product is structurally related to the ' pentacyclic ' steroid analogue (12) obtained by building an extra ring on to ring A.[10] The known preference for Δ^2-enolic derivatives in *trans*-decalin systems[11] ensures that the tricyclic compound, like the pentacyclic steroid, belongs



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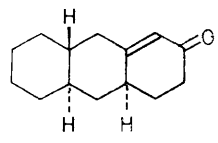

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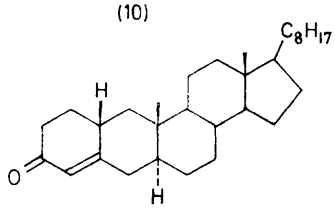

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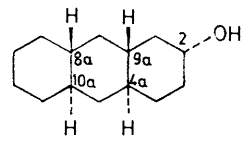
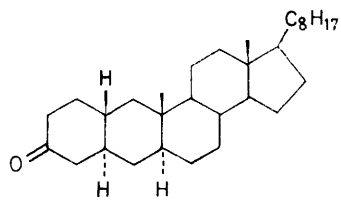


(14)
2*R*, 4a*S*, 8a*R*, 9a*R*, 10a*R*



(15)

to the perhydroanthracene rather than the perhydrophenanthrene series. As with the analogous steroid,[10] reduction of the tricyclic enone with lithium–ammonia gave the *trans*-fused saturated ketone (3) (racemic).

[7] N. M. Mitra and W. H. Elliot, *J. Org. Chem.*, 1969, **34**, 2170.
[8] S. F. Mason, *Quart. Rev.*, 1963, **17**, 20.
[9] W. Acklin, V. Prelog, F. Schenker, B. Serdarevic, and P. Walter, *Helv. Chim. Acta*, 1965, **48**, 1785; H. Dutler, M. J. Coon, A. Kull, H. Vogel, G. Waldvogel, and V. Prelog, *Eur. J. Biochem.*, 1971, **22**, 203.
[10] J.-C. Bloch and G. Ourisson, *Bull. Soc. chim. France*, 1964, 3018.
[11] D. N. Kirk and M. P. Hartshorn, ' Steroid Reaction Mechanisms,' Elsevier, Amsterdam, 1968, p. 162.

The androstenecarboxylate derivative of the derived equatorial tricyclic alcohol afforded one diastereoisomer (13) of constant m.p. after multiple fractional crystallisation: the more soluble diastereoisomer could not be purified. Reduction of the pure ester with lithium aluminium hydride gave the tricyclic alcohol (14), which was oxidised to the corresponding (−)-ketone. The ketone was shown to have the absolute configuration (3) from its negative ($n \longrightarrow \pi^*$) Cotton effect, corresponding in sign to that of the *trans*-2-decalone (2). The ketone (3) is believed to be of high optical purity, because the magnitude of the Cotton effect ($\Delta\varepsilon$ −1·64 in dioxan) was only slightly smaller than the unusually large value (reported [10] +1·83; our value +1·73 in dioxan) for the saturated ketone (15) of similar relative but opposite absolute configuration, obtained by reduction of the pentacyclic steroidal enone (12). Moreover, this $\Delta\varepsilon$ value is too large to be compatible with a *cis*-configuration at the 4a- and 9a-positions (*cf.* the small $\Delta\varepsilon$ values reported [10] for the corresponding pentacyclic steroidal ketones with *cis*-junctions at the corresponding position).

The optical purity of all the present products rests upon the criteria of constancy of m.p.s of the 3β-acetoxyandrostenecarboxylates of the alcohols, and c.d. data for the ketones. Neither D-line optical rotations nor c.d. data for the esters showed sufficient differences between diasteroisomers to be useful as further checks on the efficiency of resolutions. The n.m.r. spectra of the racemic and the optically active perhydroanthracenones were examined with the addition of optically active europium shift reagents,[12] but no resolution of signals due to enantiomeric ketones was detectable.

EXPERIMENTAL

Alumina was Spence grade H; 'deactivated alumina' refers to grade H treated with 5% of aqueous 10% acetic acid. I.r. spectra were obtained for KBr discs, u.v. spectra for solutions in ethanol, and n.m.r. spectra for solutions in carbon tetrachloride.

(±)-trans-2eq-*Decalol* (5) (*racemic*).—(*a*) 'Decahydro-2-naphthol' (Aldrich) (21·7 g) was heated with Raney nickel (B.D.H.) (3 g) for 63 h at 165—180°. The catalyst was filtered off and washed with ethanol, and the filtrate was distilled under reduced pressure. The fraction (8·3 g) of b.p. 112—120° at 17 mmHg contained naphthalene (20%), (±)-*trans*-2-decalone (60%), and the required decalol (15%) (g.l.c.). This mixture (4 g) in dry ether (350 ml) was reduced with lithium aluminium hydride (700 mg) under reflux for 1 h. The usual work-up gave a crude product (3·96 g) which afforded pure (±)-*trans*-2*eq*-decalol (2 g), m.p. 72° (lit.,[13] 72°) (from hexane at −15°).

(*b*) 'Decahydro-2-naphthol' (22·7 g) in 'decalin' (30 ml; b.p. 171—173°) was heated under reflux for 24 h with Raney nickel (3 g). Chromatography of the products on alumina (400 g) gave, after elution of hydrocarbons with hexane, a mixture of 2-decalones (mainly *trans*; 7·0 g), eluted by toluene–ethyl acetate (9 : 1), and a mixture of 2-decalols (9·5 g), eluted by ethyl acetate. Crystallisation of the 2-decalol fraction from hexane at −15°, gave (±)-*trans*-2*eq*-decalol (3·4 g), m.p. 72°.

trans-2eq-*Decalyl Esters* (6) *and* (7) *of* 3β-*Acetoxyandrost*-5-*ene*-17β-*carboxylic Acid*.—3β-Acetoxyandrost-5-ene-17β-carboxylic acid [14] (3·53 g) in thionyl chloride (14 ml) was stirred at room temperature for 4 h, then the excess of thionyl chloride was removed on the steam-bath under reduced pressure. The crude acid chloride, in pyridine (14 ml), was mixed at 0° with a solution of (±)-*trans*-2*eq*-decalol (1·51 g) in pyridine (3 ml). After 24 h at room temperature the mixture was poured into an ice-cold solution of conc. hydrochloric acid (50 ml) in water (275 ml), and the precipitated product was extracted with benzene. The crude esters (4·7 g) were chromatographed on alumina (90 g). Elution with benzene–ether gave the mixed diastereoisomeric esters (2·66 g). Nine successive crystallisations of this material from absolute ethanol at 0° gave the *ester* (6) of the (2*R*,9*R*,10*R*)-decalol (5) (180 mg), m.p. 184—184·5°; $[\alpha]_D^{28}$ −13·6 ± 0·6° (*c* 1·5 in $CHCl_3$); c.d $\Delta\varepsilon$ +3·21 (216 nm) (Found: C, 77·4; H, 9·5. $C_{32}H_{48}O_4$ requires C, 77·4; H, 9·7%). Further fractional recrystallisations of the residual material yielded an additional 56 mg of the ester (6). The last two crystallisations gave products with unchanged m.p.

The mother liquors from the first two of the second set of crystallisations were evaporated to dryness. The residues, after crystallisation twice from acetone at −80°, then five times from acetone in an ice–salt bath, and five times from methanol at 0°, yielded the *ester* (7) of (2*S*,9*S*,10*S*)-*trans*-2-decalol, m.p. 152—152·5° (the last two crystallisations did not change the m.p. of the ester), $[\alpha]_D^{28}$ −15·0 ± 0·6° (*c* 1·4 in $CHCl_3$); $\Delta\varepsilon$ +3·17 (217 nm) (Found: C, 77·3; H, 9·5%).

(+)-(2*R*,9*R*,10*R*)-trans-2-*Decalol* (5).—The ester (6) (216 mg) in dry ether (20 ml) was treated with lithium aluminium hydride (200 mg) for 2 h at room temperature. The usual work-up gave a solid product containing 21-norpregn-5-ene-3β,20-diol, from which the decalol was extracted with pentane. Sublimation (100° at 15 mmHg) gave (+)-*trans*-2-decalol (51 mg), m.p. 72°, $[\alpha]_D^{23}$ +1·35 ± 0·15° (*c* 2·6 in EtOH); $[\alpha]_D^{21}$ +1·00 ± 0·1° (*c* 1·8 in $CHCl_3$) {lit.,[13] m.p. 72°; $[\alpha]_D$ +0·7° (benzene)}.

(−)-(2*S*,9*S*,10*S*)-trans-2-*Decalol* [*Enantiomer of* (5)].—The ester (7) (126 mg) was reduced as for (6) (100 mg) to give (−)-*trans*-2-decalol (30 mg), m.p. 71—72°, $[\alpha]_D^{23}$ −1·35 ± 0·15° (*c* 2·6 in EtOH) (lit.,[13] $[\alpha]_D$ −0·7° in benzene).

(−)-(9*R*,10*R*)-trans-2-*Decalone* (2).—(+)-(2*R*,9*R*,10*R*)-*trans*-2-Decalol (5) (110 mg) in acetic acid (2 ml) was treated with chromic oxide (80 mg) for 17 h at room temperature. The *trans*-2-decalone, extracted with hexane, was an oil (93 mg), homogeneous by g.l.c., which solidified at 0°; $[\alpha]_D^{23}$ −50 ± 1° (*c* 0·85 in $CHCl_3$) (lit.,[13] $[\alpha]_D$ −53° in benzene); $\Delta\varepsilon$ −1·37 (290 nm) in MeOH; −1·12 (297) and −0·54 (190) in hexane.

(±)-trans-1eq-*Decalol* (8) (*racemic*).—Technical (±)-1-decalones (25 g) in methanol (700 ml) and conc. sulphuric acid (1 ml) were heated under reflux for 24 h. Extraction with hexane, and distillation (b.p. 115—118° at 21 mmHg), gave a product (21 g) which crystallised on cooling (90% *trans*-1-decalone by g.l.c.). The crude (±)-*trans*-1-decalone (21 g) was reduced with sodium borohydride (2·1 g) in ethanol (200 ml) at room temperature for 65 h, and after extraction with hexane gave a mixture of 1-decalols, in

[12] H. L. Goering, J. N. Eikenberry, and G. S. Koermer, *J. Amer. Chem. Soc.*, 1971, **93**, 5913; R. R. Fraser, M. A. Petit, and J. K. Saunders, *Chem. Comm.*, 1971, 1450.

[13] R. Mislin, Dissertation, E.T.H., Zürich, 1968.

[14] J. Staunton and E. J. Eisenbraun, *Org. Synth.*, 1962, **42**, 4.

which (8) was preponderant (g.l.c.). Three crystallisations from ether at −15° gave pure (±)-*trans*-1*eq*-decalol, m.p. 60—61°.

trans-1eq-*Decalyl* 3β-*Acetoxyandrost*-5-*ene*-17β-*carboxylate* (9).—3β-Acetoxyandrost-5-ene-17β-carboxylic acid (7·83 g) was converted into the acid chloride, as before, and treated in pyridine (20 ml) with *trans*-1*eq*-decalol (3·36 g) in pyridine (20 ml). After 24 h at room temperature the ester was isolated as before. The crude product (10·47 g) was chromatographed on alumina (220 g). Elution with benzene–ether (9 : 1) gave a mixture of the diastereoisomeric esters (4·72 g). Ten crystallisations from ethanol gave the *diastereoisomer* (9) (1·42 g), m.p. 166·5—167°, unchanged by the two final crystallisations; $[\alpha]_D^{23}$ +0·8 ± 0·2° (*c* 0·57 in $CHCl_3$); Δε +1·74 (216 nm) (Found: C, 77·6; H, 9·5. $C_{32}H_{48}O_4$ requires C, 77·4; H, 9·7%).

(+)-(1*S*,9*S*,10*R*)-trans-1-*Decalol* (8).—The ester (9) (1·00 g) was reduced in ether (150 ml) with lithium aluminium hydride (220 mg) for 4 h at room temperature. The usual work-up, followed by extraction with isopentane and sublimation (100° and 12 mmHg), gave (+)-*trans*-1-decalol (8) (270 mg), m.p. 78—79° (lit.,[9] 81°); $[\alpha]_D^{23}$ +40 ± 1° (*c* 0·75 in $CHCl_3$); $[\alpha]_D^{23}$ +40 ± 1° (*c* 0·6 in EtOH) (lit.,[10] +48° in EtOH).

(−)-(9*S*,10*R*)-trans-1-*Decalone* (1).—Oxidation of the foregoing 1-decalol (171 mg) as reported [9] gave (−)-*trans*-1-decalone (149 mg), m.p. 43° (lit.,[9] 43°); $[\alpha]_D^{22}$ −10 ± 1° (*c* 0·5 in EtOH) (lit.,[9] −10° in EtOH); Δε +0·95 (292 nm) in MeOH; +0·81 (296) and +3·6 (188) in hexane.

(±)-trans,syn,trans-*Perhydroanthracen*-2-*one* (3) (*racemic*).—(±)-*trans*-2-Decalone (15 g) and pyrrolidine (9 ml) in benzene (50 ml) were heated under reflux (Dean–Stark water trap) for 18 h, then the solvents were removed under reduced pressure to yield the crude enamine (10) (22·2 g). A solution of this enamine in anhydrous dioxan (60 ml) was treated at 0° with freshly distilled but-3-en-2-one (12 ml), then the mixture was left at room temperature for 18 h, and finally warmed at 50° for 30 min. The solution was made just acid with 4N-hydrochloric acid and heated under reflux for 1 h. Dilution with water and extraction with ether afforded a crude product (20·3 g) which was chromatographed on silica gel (400 g). Elution with benzene and benzene–ether afforded a series of fractions, which were examined by t.l.c. Fractions eluted with benzene–ether (9 : 1 and 7 : 3) contained the required enone (11) (u.v. absorption near 240 nm) and were combined (13·2 g, crude).

The enone was not purified at this stage, but the crude material (13·2 g) in tetrahydrofuran (200 ml) was added to a solution of lithium (2 g) in liquid ammonia (200 ml), and the mixture was stirred for 1 h. The product (13·1 g), isolated by use of ether, was a mixture containing the tricyclic alcohol (14) and the ketone (3) (t.l.c.). It was oxidised by stirring for 4 h in acetic acid (150 ml) at room temperature with chromic oxide (7 g) in water (7 ml). Extraction by use of ether gave the crude ketone (3) (11·6 g), which was chromatographed on alumina (500 g). The saturated ketone (3) was eluted by benzene–ether (95 : 5, 90 : 10, and 80 : 20) (total weight 3·5 g). Crystallisation from ether at −70° afforded the pure (±)-*ketone* (1·7 g), m.p. 81—82°, $\nu_{max.}$ 1715 cm^{-1} (Found: C, 81·7; H, 10·6. $C_{14}H_{22}O$ requires 81·5; H, 10·75%).

Later fractions, eluted with benzene containing increasing proportions of ether, gave the enone (11) (4·4 g, crude), which crystallised from ether at −70° to give the (±)-*tricyclic enone* (1·8 g), m.p. 74—75°, $\nu_{max.}$ 1666 and 1620 cm^{-1}, $\lambda_{max.}$ 241 nm (ε 16,000), τ 4·25 (>C=CH–) (Found: C, 82·5; H, 9·9. $C_{14}H_{20}O$ requires C, 82·3; H, 9·9%).

(±)-trans,syn,trans-*Perhydroanthracen*-2eq-*ol* (14) (*racemic*).—The tricyclic ketone (3) (2·07 g) in ethanol (25 ml) was stirred for 2 h with sodium borohydride (250 mg) at room temperature. Extraction with ether gave the crude alcohol (14) (2·07 g), containing a little of the axial hydroxy-isomer (g.l.c.). Crystallisation from ether at −5° gave the (±)-2*eq*-alcohol (14) (1·2 g). Oxidation of the residues with chromic oxide and repetition of the reduction with sodium borohydride gave a further quantity (0·57 g) of the required alcohol, m.p. 164°, $\nu_{max.}$ 3250—3180, 1050, and 1027 cm^{-1}; τ 6·47 (*W* 25 Hz, C*H*OH) (Found: C, 80·8; H, 11·3. $C_{14}H_{24}O$ requires C, 80·7; H, 11·6%).

3β-*Acetoxyandrost*-5-*ene*-17β-*carboxylate* (13) *of the Tricyclic Alcohol* (14).—The acid chloride, prepared as before from the steroid acid (3·7 g), was added in pyridine (20 ml), at 0° to the (±)-tricyclic alcohol (14) (racemic) (1·71 g) in pyridine (10 ml). After 24 h at room temperature the product was isolated with chloroform. Removal of the solvent afforded the crude esters (5·29 g), which were chromatographed on alumina (200 g). Elution with benzene–ether gave no separation of the diastereoisomeric esters, so the combined fractions (4·21 g) were crystallised twelve times from ethyl acetate to give the *ester* (13) of the alcohol (14) (158 mg). The two final crystallisations did not change the product, m.p. 230—231°; Δε +4·7 (214 nm) in dioxan; $[\alpha]_D^{28}$ −9° ± 1° (*c* 0·5 in $CHCl_3$); $\nu_{max.}$ 1735, 1725, and 1245 cm^{-1} (Found: C, 78·4; H, 9·6. $C_{36}H_{54}O_4$ requires C, 78·5; H, 9·9%).

(−)-(4aS,8aR,9aR,10aR)-trans,syn,trans-*Perhydroanthracen*-2-*one* (3), *and* (2R,4aS,8aR,9aR,10aR)-trans,syn,-trans-*Perhydroanthracen*-2-*ol* (14).—The foregoing ester (13) (134 mg) was reduced with lithium aluminium hydride (90 mg) in ether (200 ml) for 16 h at room temperature. Extraction of the product by use of ether gave an equimolar mixture (130 mg) of the tricyclic alcohol (14) and 21-norpregn-5-ene-3β,20-diol. A portion (65 mg) of this mixture was oxidised in acetic acid (17 ml) with chromic oxide (160 mg) in water (1 ml) for 4 h at room temperature. Chromatography of the extracted products on alumina (5 g), and elution with benzene–ether (9 : 1), gave the (−)-*tricyclic ketone* (3) (18 mg; after sublimation at 100° and 15 mmHg), m.p. 110—111°, $[\alpha]_D^{25}$ −30 ± 2° (*c* 0·4 in $CHCl_3$); i.r. and n.m.r. spectra and g.l.c. behaviour identical with those of the racemic ketone; Δε −1·86 (290 nm) in MeOH, −1·37 (297) and +1·5 (185) in hexane. The remainder of the mixture (65 mg) was chromatographed on deactivated alumina (2 g). Benzene eluted a trace of oil, then benzene–ethyl acetate (10 : 1) eluted the *tricyclic alcohol* (14) (20·2 mg), m.p. 162·5—163° (from ether–hexane); $[\alpha]_D^{28}$ +0·5 ± 0·5° (*c* 1·0 in $CHCl_3$). (The small amount available did not permit a more accurate determination.) The i.r. spectrum and g.l.c. behaviour were identical with those of the racemic alcohol.

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