

Synthesis of Annulated 10-Methyloctalones by Epoxyolefin Cyclisation

By Peter Marsham and David A. Widdowson, Chemistry Department, Imperial College, London SW7
James K. Sutherland,* Chemistry Department, The University, Manchester M13 9PL

Boron trifluoride-ether catalysed cyclisation of 2-[2-(cyclohex-1-enyl)ethyl]-1,2-epoxy-4,4-ethylenedioxy-1-methylcyclohexane (4) yields, after hydrolysis, a mixture of ketols (12) which probably have steroid geometry at C-9 and C-10. Cyclisation of 5,10-epoxy-3,3-ethylenedioxy-18-nor-9,10-secoandrost-8-ene (4a) yields some 18-norsteroid products (12a) but is complicated by (4a) being a mixture of isomers.

In order to extend a previously developed synthesis of *trans*-hydrindane derivatives¹ to the fabrication of the steroid nucleus we have investigated the acid catalysed cyclisation of olefin epoxides as a method

formation of the 8-9 double bond and of the 5,10-epoxide. As one solution to the latter problem we investigated the epoxidation of (3) which was prepared from the known anisole² † (1) *via* Birch reduction to the enol-ether (2), hydrolysis to the corresponding ketone with aqueous oxalic acid, and acetalisation with ethylene glycol. Disappointingly, the epoxidation of (3) with *m*-chloroperbenzoic acid was not highly selective and after t.l.c. on silver nitrate-silica gel the required epoxide (4) (20%), the isomer (5) (12%), and the diepoxide (6) (10%) were isolated.

In an effort to overcome this lack of selectivity we attempted to modify the synthesis of (4); the alcohol ‡ (7) was converted into the acetal (8) by a procedure similar to that applied to (1). The bromide (9) was prepared from the alcohol (8) (carbon tetrabromide-tri-*n*-butylphosphine⁴), and reaction of the Grignard reagent derived from it with cyclohexanone yielded the alcohol (11), but the best yield obtainable was only 10%; that the organometallic reagent was being formed in good yield was established by deuteration which generated the monodeuterio-compound (10) in good yield. Why it is appreciably less reactive than the Grignard reagent derived from (7) is a matter for speculation.

In the event, the most efficient method for preparing (4) would not allow regiospecific generation of the double bond when applied to an unsymmetrical ketone. The alcohol (7) was converted into the chloride and the derived Grignard reagent reacted with cyclohexanone to yield the known adduct (65%) which was transformed to the alcohol (11) (90%) by the Birch reduction procedure used for the preparation of (3). Epoxidation of (11) gave the corresponding epoxide (90%) which was dehydrated with methanesulphonyl chloride in pyridine to give (4) (55%).

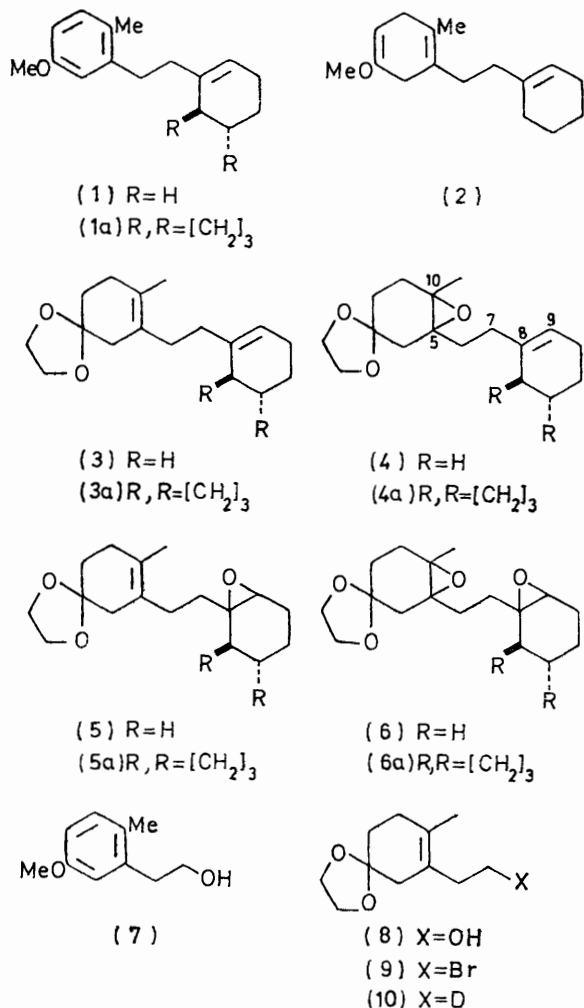
The epoxide (4) was treated with a number of Lewis and protonic acids, the most successful being boron trifluoride-ether in methylene chloride; from this reaction, after hydrolysis with acetone-water-toluene-*p*-sulphonic acid, the crystalline mixture of ketols § (12) could be isolated in 96% yield. The alternative structure for (12) (five-membered ring B) was excluded since treatment of (12) with sodium ethoxide in ethanol gave an $\alpha\beta$ -unsaturated ketone chromophore, λ_{\max} .

¹ D. Duffin and J. K. Sutherland, *Chem. Comm.*, 1970, 627.

² A. Higginbottom, P. Hill, and W. F. Short, *J. Chem. Soc.*, 1937, 263.

³ (a) C. L. Hewett, *J. Chem. Soc.*, 1936, 51; (b) J. W. Cook, C. L. Hewett, and A. M. Robinson, *ibid.*, 1939, 168.

⁴ J. B. Lee and T. J. Nolan, *Canad. J. Chem.*, 1966, **44**, 1331.



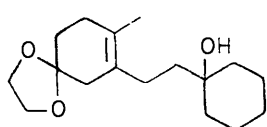
of annulation. It is clear that any synthesis of the precursor to cyclisation (4) from a hydrindanone requires 7-8 bond formation and methods for the regiospecific

† This compound is best prepared from 3-bromo-4-methylanisole following the route described for the nor-methyl compound.^{3a}

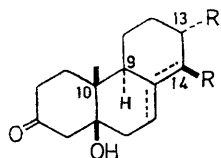
‡ Prepared by the method used for the nor-methyl compound^{3b} and characterised as its 3,5-dinitrobenzoate, m.p. 148–151°.

§ All compounds reported containing chiral centres are racemic; in the discussion of the a series only the 10 β -enantiomers are considered.

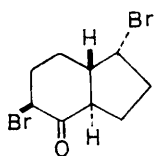
233 nm. The stereochemistry indicated is assigned on the basis of *trans*-diaxial opening of the epoxide ring and a chair-like transition-state for the cyclisation.



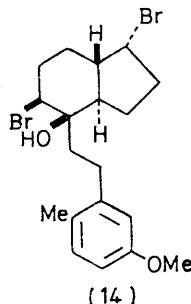
(11)



(12) R = H

(12a) R, R = -[CH₂]₃

(13)



(14)

The work of Johnson⁵ and others on polyolefin cyclisation reveals that reaction in chair conformations is overwhelmingly preferred, but in the related olefin-epoxide cyclisations⁶ the evidence is less strong. When cyclisation is terminated by addition to certain conformationally locked cyclohexenes, *e.g.* (4a) an additional stereochemical factor arises since axial attack could only occur *via* a boat-like transition state. There are few exceptions to the rule of cyclisation *via* a chair-like transition state, but there are numerous exceptions⁷ to a rule of axial attack when a cyclohexylidene derivative with an *sp*² hybridised carbon is formed. Thus it is likely that cyclisation of the β -epoxide of (4a) would generate steroid geometry.

In an attempt to explore this point the bromoketone⁸ (13) was treated with the Grignard derived from the chloride of (7) to yield the bromohydrin* (14) (45%). Reduction of (14) with zinc in acetic acid gave the olefin (1a) (75%) which was converted by a modification of the previous procedure into (3a). Again epoxidation of the diene with *m*-chloroperbenzoic acid was unselective, yielding (4a) (21%), (5a)† (21%), and (6a) (14%), together with some starting material. Reaction of (4a) with boron trifluoride-ether gave, after hydrolysis, a crystalline substance, m.p. 138–139° (45%; 24% isolated by direct crystallisation); however the n.m.r. spectrum clearly indicated that it was a mixture of at least three substances, τ (CDCl₃) 9.05 (s), 9.08 (s), 9.16 (s), and 4.70 (½H). On treatment with sodium ethoxide in ethanol the ketols were converted into the corresponding $\alpha\beta$ -unsaturated ketones, λ_{\max} .

* This compound does not form an epoxide on reaction with base, hence the stereochemistry assigned.

† This oxide is obtained in excellent yield by sequential reaction of (3a) with acetone-water-*N*-bromosuccinimide and sodium carbonate-methanol.

(EtOH) 230 nm, characterised as a 2,4-dinitrophenyl-hydrazone mixture.

The cyclisation of racemic (4) is much more efficient than that of (4a); this is almost certainly due to (4a) being a mixture of diastereoisomeric α - and β -5,10-epoxides. The possible geometries of reaction and their stereochemical consequences for the epoxides are summarised in the Table. The postulate that (4) is

Relative stereochemistry (to 13 β -H) of starting material and product from cyclisation modes

| Epoxide (4a) | Transition state | 10-Me | 9-H |
|--------------|------------------|----------|----------|
| β | Chair | β | α |
| β | Boat | β | β |
| α | Chair | α | β |
| α | Boat | α | α |

cyclising *via* a chair-like transition state and that C(10)-Me and C(9)-H are in an antiperiplanar relationship receives some support from $W_{\frac{1}{2}}$ (9-Me) – $W_{\frac{1}{2}}$ (Me₄Si) being *ca.* 0.55 Hz for each of the methyls in (12); only in that geometry is there a hydrogen to account for this long-range *W*-coupling.⁹ Again, if it is accepted that the three methyls in (12a) represent only three compounds the couplings indicate that anti-periplanar substituents at 9 and 10 are being generated from both epoxides. To summarise, it appears that this method of annulation is efficient and stereospecific at the ring junction when applied to simple systems, but application to the steroid series would require a stereo- and regio-specific method for preparing the epoxide precursors.

EXPERIMENTAL

Unless otherwise noted reactions were worked up by addition of water, extracting with ether, washing the extract with saturated aqueous sodium hydrogen carbonate and water, and then drying and concentrating the extract. N.m.r. spectra were measured at 60 MHz in CCl₄ unless indicated otherwise.

2-[2-(Cyclohex-1-enyl)ethyl]-4-methoxy-1-methylcyclohexa-1,4-diene (2).—Sodium metal (1.7 g) was added in small portions to a stirred solution of the ether (1) (674 mg) in distilled ammonia (*ca.* 50 ml), tetrahydrofuran (25 ml), and *t*-butyl alcohol (25 ml). Stirring was continued for 5 h, excess of powdered ammonium chloride was added and the ammonia was allowed to evaporate overnight. Work-up gave the cyclohexadiene (2) (616 mg, 92%), as a pale yellow oil. An analytically pure sample was obtained by chromatography on grade III alumina, eluting with pentane, ν_{\max} (film) 1700, 1670, and 800 cm⁻¹, τ 4.66 (1H, m), 5.58 (1H, m), 6.55 (3H, s), and 8.40 (3H, s) (Found: C, 82.8; H, 10.3. C₁₆H₂₄O requires C, 82.8; H, 10.4%).

⁵ W. S. Johnson, *Accounts Chem. Res.*, 1968, **1**, 1.

⁶ D. J. Goldsmith, *J. Amer. Chem. Soc.*, 1962, **84**, 3913; D. J. Goldsmith, B. C. Clark, and R. C. Jones, *Tetrahedron Letters*, 1967, 1211; E. E. van Tamelen, *Accounts Chem. Res.*, 1968, **1**, 111; E. D. Brown and J. K. Sutherland, *Chem. Comm.*, 1968, 1060; E. E. van Tamelen, R. A. Holton, R. E. Hopla, and W. E. Konz, *J. Amer. Chem. Soc.*, 1972, **94**, 8228.

⁷ L. Velluz, J. Valls, and G. Nominé, *Angew. Chem. Internat. Edn.*, 1965, **4**, 181.

⁸ W. Heggie, D.I.C. Thesis, Imperial College, 1970.

⁹ L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' 2nd edn., 1969, p. 337, and references therein.

3-[2-(Cyclohex-1-enyl)ethyl]-4-methylcyclohex-3-enone.— A solution of the enol ether (2) (228 mg) and oxalic acid (250 mg) in ethanol (15 ml) and water (3 ml) was stirred overnight. Aqueous sodium hydrogen carbonate was added to neutralise the acid and work-up gave the cyclohexenone (193 mg), as a pale yellow oil, ν_{\max} (film) 1720 and 1670 cm^{-1} , τ 4.74 (1H, m) and 7.67 (3H, s), characterised as its *semicarbazone*, m.p. 153–155° (ethanol) (Found: C, 69.8; H, 9.1; N, 15.3. $\text{C}_{16}\text{H}_{25}\text{N}_3\text{O}$ requires C, 69.8; H, 9.1; N, 15.3%).

2-[2-(Cyclohex-1-enyl)ethyl]-4,4-ethylenedioxy-1-methylcyclohexene (3).—A solution of the ketone (114 mg), ethylene glycol (1 ml), and toluene-*p*-sulphonic acid (10 mg) in benzene (10 ml) was stirred overnight under reflux with a Dean-Stark separator to remove the water produced. Work-up gave the *ethylenedioxy*cyclohexene (3) (138 mg) as an oil. P.l.c. (alumina; petroleum b.p. 60–80°), gave an analytically pure sample, τ 4.60 (1H, m) and 6.10 (4H, s) (Found: C, 77.9; H, 9.9. $\text{C}_{17}\text{H}_{26}\text{O}_2$ requires C, 77.9; H, 9.9%).

4,4-Ethylenedioxy-2-(2-hydroxyethyl)-1-methylcyclohexene (8).—Sodium metal (48 g) was added in small portions over 30 min to a stirred solution of the alcohol (7) (17 g) in distilled ammonia (ca. 500 ml), tetrahydrofuran (200 ml), and *t*-butyl alcohol (200 ml). After stirring for a further 5 h the reaction was worked up as before to give an alcohol (15.9 g, 93%), as a pale yellow oil, ν_{\max} (film) 3450, 1690, and 1670 cm^{-1} , τ 5.55 (1H, m), 6.50 (2H, t, *J* 6.5 Hz), 7.78 (2H, t, *J* 6.5 Hz), 6.58 (3H, s), and 8.35 (3H, s). The alcohol (13.3 g) in benzene (350 ml) was stirred overnight with ethylene glycol (70 ml) and toluene-*p*-sulphonic acid (2 g). The solution was poured into excess of aqueous sodium hydrogen carbonate, and the benzene layer separated and washed with water. The combined aqueous solutions were extracted with more benzene (200 ml). The combined benzene solutions were dried and evaporated. Fractional distillation *in vacuo* gave the alcohol (8) (7.12 g.), b.p. 110–114° at 0.02 mmHg. Losses on distillation were minimised by bulb to bulb distillation at 150° (bath) and 5×10^{-4} mmHg. In a typical distillation 1.48 g crude material gave 1.34 g purified alcohol, ν_{\max} (film) 3450 cm^{-1} , τ 6.15 (4H, s), 6.50 (2H, t, *J* 6.5 Hz), and 8.35 (3H, s), which was characterised as its 3,5-dinitrobenzoate (oil) (Found: C, 55.4; H, 5.2; N, 7.2. $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}_8$ requires C, 55.1; H, 5.1; N, 7.1%).

4,4-Ethylenedioxy-2-(2-bromoethyl)-1-methylcyclohexene (9).—A solution of the alcohol (8) (713 mg), carbon tetrabromide (1.2 g), and pyridine (10 drops) in benzene (5 ml) was stirred during the dropwise addition of tri-*n*-butylphosphine (800 mg) in benzene (5 ml). The solution was stirred under reflux for 2 h, powdered lithium bromide (1.5 g) was added, and after a further 2 h reflux, the solution was allowed to cool overnight. P.l.c. of the crude product (silica gel; 1:1 methylene chloride-petroleum b.p. 60–80°) gave the *bromo-compound* (9) (484 mg, 52%), as an oil, τ 6.15 (4H, s), 6.74 (2H, t, *J* 8 Hz), 7.52 (2H, t, *J* 8 Hz), and 8.35 (3H, s) (Found: C, 50.8; H, 6.5. $\text{C}_{11}\text{H}_{17}\text{BrO}_2$ requires C, 50.6; H, 6.6%).

1-[2-(5,5-Ethylenedioxy-2-methylcyclohex-1-enyl)ethyl]-cyclohexanol (11).—(a) To a solution of the Grignard reagent from the bromide (9) (470 mg) and magnesium turnings (100 mg) in tetrahydrofuran (10 ml) was added cyclohexanone (700 mg) in tetrahydrofuran (5 ml) and the solution was refluxed overnight under nitrogen. T.l.c. of the crude product showed a complex mixture. P.l.c.

gave the alcohol (11) (50 mg, 10%), as an oil, ν_{\max} (film) 3500 cm^{-1} , τ (CDCl_3) 6.05 (4H, s), characterised as its 2,4-dinitrophenylhydrazone, m.p. 151–152° (methylene chloride-petroleum b.p. 60–80°) (Found: C, 60.5; H, 6.8; N, 13.3%; M^+ , 280. $\text{C}_{21}\text{H}_{28}\text{N}_4\text{O}_5$ requires C, 60.6; H, 6.8; N, 13.5%; M , 280).

A solution of the Grignard reagent was prepared from the bromide (9) (178 mg) and magnesium turnings (100 mg) in tetrahydrofuran (4 ml) under nitrogen. Deuterium oxide (0.5 ml) was added dropwise to the stirred solution. After 15 min, work-up gave 2-([2- ^2H]ethyl)-4,4-ethylenedioxy-1-methylcyclohexene (10) (118 mg), as an oil, τ 6.15 (4H, s), 8.03 (2H, t, *J* 8 Hz), and 9.10 (2H, t, *J* 8 Hz) (Found: M^+ , 183. $\text{C}_{11}\text{H}_{17}\text{DO}_2$ requires M , 183). The protio-analogue was characterised as its 2,4-dinitrophenylhydrazone, m.p. 159–161° (cyclohexane) (Found: C, 56.6; H, 5.2; N, 17.6. $\text{C}_{15}\text{H}_{18}\text{N}_4\text{O}_4$ requires C, 56.6; H, 5.7; N, 17.6%).

(b) Sodium metal (9 g) was added in small portions to a stirred solution of 1-[2-(5-methoxy-2-methylphenyl)ethyl]-cyclohexanol (2.73 g.) in distilled ammonia (ca. 200 ml), tetrahydrofuran (80 ml), and *t*-butyl alcohol (80 ml). Stirring was continued 4 h, and the reaction was worked up as before.

The intermediate enol ether (2.47 g) in benzene (125 ml) was stirred vigorously overnight with ethanediol (25 ml) and toluene-*p*-sulphonic acid (250 mg). Work-up gave the ethylene acetal (11) (2.8 g, 90%).

(±)-2-[2-(Cyclohex-1-enyl)ethyl]-1,2-epoxy-4,4-ethylenedioxy-1-methylcyclohexane (4).—(a) *m*-Chloroperbenzoic acid (176 mg; 88% w/w) was added to a stirred solution of diene (3) (236 mg) in methylene chloride (5 ml). Stirring was continued 1 h. P.l.c. on 10% silver nitrate on silica gel (8:1 petroleum b.p. 60–80°-ethyl acetate) gave three products. The least polar (R_F ca. 0.5) was the *epoxy-olefin* (4) (50 mg, 20%), as an oil, τ 4.70 (1H, m), 6.22 (4H, s), and 8.77 (3H, s) (Found: C, 73.2; H, 9.5. $\text{C}_{17}\text{H}_{26}\text{O}_3$ requires C, 73.4; H, 9.4%). The second product (R_F ca. 0.3) was 2-[2-(1,2-epoxycyclohexyl)ethyl]-4,4-ethylenedioxy-1-methylcyclohexane (5) (31 mg), obtained as an oil, τ 6.25 (4H, s) (Found: C, 73.5; H, 9.1. $\text{C}_{17}\text{H}_{26}\text{O}_3$ requires C, 73.4; H, 9.4%). The most polar product (R_F ca. 0.1) was 1,2-epoxy-2-[2-(1,2-epoxycyclohexyl)ethyl]-4,4-ethylenedioxy-1-methylcyclohexane (6) (26 mg) obtained as an oil, τ 6.25 (4H, s) and 8.77 (3H, s) (Found: C, 69.5; H, 8.9. $\text{C}_{17}\text{H}_{26}\text{O}_4$ requires C, 69.4; H, 8.9%).

(b) The ethylene acetal (11) (2.8 g) in methylene chloride (150 ml) was stirred overnight with *m*-chloroperbenzoic acid (2.13 g; 88% w/w). Work-up gave the epoxide of (11) (2.68 g), ν_{\max} (film) 3500 cm^{-1} , τ (CDCl_3) 6.10 (4H, s) and 8.70 (3H, s). This epoxy-alcohol (128 mg) in pyridine (3 ml) was treated overnight at 0° with redistilled methanesulphonyl chloride (0.6 ml). P.l.c. (silica gel, methylene chloride) of the residue gave the epoxy-olefin (4) (66 mg).

Cyclisation of the Epoxy-olefin (4).—Boron trifluoride-ether (2 drops) was added to a stirred solution of the epoxy-olefin (4) (45 mg) in methylene chloride (4 ml) at 0° under nitrogen. After 40 min water was added and the mixture was extracted with methylene chloride. The solvent was evaporated and the crude product was refluxed 1 h with toluene-*p*-sulphonic acid (20 mg) in acetone (6 ml) and water (4 ml). The acetone was evaporated and the mixture extracted with ether. Work-up gave a waxy solid (36 mg) which crystallised on trituration with petroleum. Recrystallisation (chloroform-petroleum b.p.

60–80°) gave prisms, m.p. 136–143° of a 1 : 1 mixture of 3,4,4a,4b α ,5,6,7,8,10,10a- and 3,4,4a,4b α ,5,6,7,9,10,10a-decahydro-10a β -hydroxy-4a β -methylphenanthren-2(1H)-one (12), homogeneous on t.l.c. (silica gel; 4 : 1 methylene chloride-ether), ν_{\max} (Nujol) 3360 and 1700 cm^{-1} , τ (CDCl_3) 4.34 (0.5H, m), 4.78 (0.5H, m), 9.08 (1.5H, s), and 9.13 (1.5H, s), M^+ 234 (Found: C, 76.6; H, 9.4. Calc. for $\text{C}_{15}\text{H}_{22}\text{O}_2$: C, 76.9; H, 9.5%).

(\pm)-17 α ,9 β -Dibromo-8 β -hydroxy-3-methoxy-18-nor-9,10-secoandrosta-1,3,5(10)-triene (14).—A solution of the Grignard reagent was prepared from magnesium turnings (360 mg, activated with a few drops of 1,2-dibromoethane) and the chloride of (7) (2.8 g) in refluxing tetrahydrofuran (50 ml). It was filtered under nitrogen and added dropwise to a stirred solution of the dibromoketone (13) (2.2 g) in ether (50 ml). Stirring was continued overnight, and after work-up the dibromohydrin (14) (1.424 g, 45%), a viscous oil, was obtained by chromatography (silica gel; 1 : 1 methylene chloride-petroleum b.p. 60–80°). An analytically pure sample was obtained by short path distillation [100° (bath) at 10^{-4} mmHg], ν_{\max} (CHCl_3) 3550 cm^{-1} , τ (CDCl_3) 2.8–3.6 (3H, m), 5.6–6.0 (2H, m), 6.28 (3H, s), and 7.76 (3H, s), M^+ 444/446/448 (Found: C, 51.2; H, 5.8. $\text{C}_{19}\text{H}_{26}\text{Br}_2\text{O}_2$ requires C, 51.1; H, 5.8%).

(\pm)-3-Methoxy-18-nor-9,10-secoandrosta-1,3,5(10),8-tetraene (1a).—AnalaR zinc dust (1.6 g) was added to a solution of the dibromohydrin (14) (807 mg) in glacial acetic acid (30 ml) and stirred 1 h under reflux. The solution was filtered, the acetic acid was evaporated off, and the residue worked up. The extract was dissolved in petroleum and passed through a short silica gel column. Evaporation gave the olefin (1a) (361 mg, 74%) as an oil. An analytically pure sample was obtained by short path distillation [100° (bath) at 0.02 mmHg], τ (CDCl_3) 2.7–3.5 (3H, m), 4.64 (1H, m), 6.20 (3H, s), and 7.76 (3H, s), M^+ 270 (Found: C, 84.4; H, 9.5. $\text{C}_{19}\text{H}_{26}\text{O}$ requires C, 84.4; H, 9.6%).

(\pm)-3,3-Ethylenedioxy-18-nor-9,10-secoandrosta-5(10),8-diene (3a).—Sodium metal (13 g) was added in small portions to a stirred solution of the olefin (1a) (3.4 g) in distilled ammonia (ca. 200 ml), tetrahydrofuran (85 ml), and t-butyl alcohol (85 ml). Stirring was continued 5 h and the reaction was worked up as before. The intermediate enol ether (3.13 g), ethylene glycol (40 ml), and toluene-*p*-sulphonic acid (400 mg) were stirred vigorously overnight in benzene (200 ml). Work-up as before and chromatographic purification (silica gel; 4 : 1 petroleum b.p. 60–80°-methylene chloride) gave the ethylene acetal diene (3a) (2.094 g, 60%), as an oil, τ (CDCl_3) 4.76 (1H, m) and 6.06 (4H, s) (Found: M^+ , 302. $\text{C}_{20}\text{H}_{30}\text{O}_2$ requires M , 302), which was characterised as its 2,4-dinitrophenylhydrazone, m.p. 125–126° (petroleum b.p. 60–80°) (Found: C, 65.7; H, 6.9; N, 12.7. $\text{C}_{24}\text{H}_{30}\text{N}_4\text{O}_4$ requires C, 65.8; H, 6.9; N, 12.8%).

Epoxidation of the Diene (3a).—*m*-Chloroperbenzoic acid (824 mg of 88% w/w, 4.2 mmol) was added in small portions to a stirred solution of the diene (3a) (1.208 g, 4.0 mmol) in methylene chloride (40 ml) whilst maintaining the temperature below 10°. It was warmed to 25°, stirred 1 h and worked up. P.l.c. (silica gel; 8 : 1 petroleum b.p. 60–80°-ethyl acetate) separated the crude product into four compounds. The least polar compound was unchanged diene (3a) (286 mg). The second compound was (\pm)-5-10-epoxy-3,3-ethylenedioxy-18-nor-9,10-secoandrosta-8-ene (4a) (265 mg), an oil, τ (CDCl_3) 4.70 (1H, m), 6.15 (4H, s), and 8.70 (3H, s) (Found: C, 75.7; H, 9.4. $\text{C}_{20}\text{H}_{30}\text{O}_3$ requires C, 75.4; H, 9.5%). The third compound was (\pm)-8,9-epoxy-3,3-ethylenedioxy-18-nor-9,10-secoandrosta-5(10)-ene (5a) (277 mg) (Found: C, 75.4; H, 9.6. $\text{C}_{20}\text{H}_{30}\text{O}_3$ requires C, 75.4; H, 9.5%). The most polar compound was (\pm)-5,10;8,9-diepoxo-3,3-ethylenedioxy-18-nor-9,10-secoandrosta-6a (190 mg), an oil, τ (CDCl_3) 6.15 (4H, s) and 8.70 (3H, s) (Found: C, 71.7; H, 8.9. $\text{C}_{20}\text{H}_{30}\text{O}_4$ requires C, 71.8; H, 9.0%).

Cyclisation of the Epoxy-olefin (4a).—Boron trifluoride-ether (5 drops) was added to a stirred solution of the epoxy-olefin (4a) (265 mg) in methylene chloride (24 ml) at 0° under nitrogen. After 2 h at 0° water was added and the mixture extracted with methylene chloride. The solvent was removed at 20° and the residue stirred overnight with toluene-*p*-sulphonic acid (50 mg) in acetone (20 ml) and water (10 ml). Work-up yielded a semicrystalline material which on recrystallisation (methylene chloride-petroleum b.p. 60–80°) gave a mixture of 5 β -hydroxy-18-norandrosta-7-en-3-one and -8(14)-en-3-one (12a) (64 mg) as needles, m.p. 138–139°, ν_{\max} (Nujol) 3400 and 1715 cm^{-1} , τ (CDCl_3) 4.70 (m), 9.05 (s), 9.08 (s), and 9.16 (s), M^+ 274 (Found: C, 78.6; H, 9.5. Calc. for $\text{C}_{18}\text{H}_{26}\text{O}_2$: C, 78.8; H, 9.6%). P.l.c. (silica gel; 3 : 2 ether-petroleum b.p. 60–80°) of the mother liquors gave a semicrystalline material (112 mg), homogeneous on t.l.c., containing ca. 50% of (12a) (n.m.r.), which was a mixture of several ketones (ν_{\max} 1730, 1720, 1715, 1695, and 1660 cm^{-1}).

A solution of the ketols (12a) (5.1 mg) in ethanol (1 ml) was treated for 1 h with sodium ethoxide (from 9.1 mg sodium metal). Work-up yielded a mixture of 18-norandrosta-4,7-dien-3-one and -4,8(14)-dien-3-one (4.1 mg) as an oil, ν_{\max} (CHCl_3) 1655 cm^{-1} , λ_{\max} (EtOH) 230 nm., characterised as the 2,4-dinitrophenylhydrazone mixture, orange plates, m.p. 225–227° (petroleum b.p. 60–80°) (Found: C, 66.0; H, 6.5; N, 12.9. Calc. for $\text{C}_{24}\text{H}_{28}\text{N}_4\text{O}_4$: C, 66.1; H, 6.4; N, 12.9%).

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