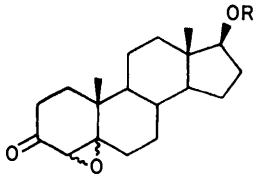
A Mild and Efficient Degradation of Ring *A* of Steroids

By **Robin B. Boar,* Susan L. Jones,** and **Arvind C. Patel,** Department of Chemistry, Chelsea College, London SW3 6LX

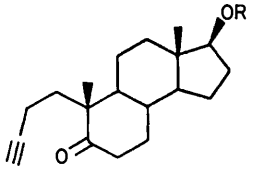
17β-Acetoxy-4,5-secoandrost-3-yn-5-one and 4,5-secopregn-3-yne-5,20-dione, readily available by Eschenmoser–Tanabe fragmentation, have been rearranged to the corresponding 2-ynes, which were then cleaved to afford 2,5-seco-3,4-dinor-derivatives in excellent overall yield. The release of toluene-*p*-sulphinic acid during the fragmentation step can lead to the acetylation sulphinylation of an extraneous hydroxy-group. The active sulphinylating species is evidently *p*-tolyl toluene-*p*-sulphinyl sulphone.

In connection with the synthesis of $^{13}C_2$-labelled steroids for use in metabolic studies we required a mild yet efficient method for the removal of two adjacent carbon atoms from the steroid nucleus. We report herein a route for the conversion of steroidal 4-en-3-ones into 2,5-seco-3,4-dinor-derivatives under conditions which are compatible with various functional groups in other parts of the molecule.

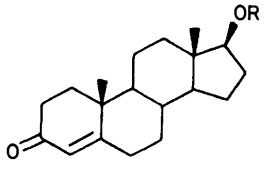
Most previous degradations of ring *A* of steroids have employed a direct oxidation, often under necessarily vigorous conditions, for the initial cleavage of ring *A*.[1] The efficient fragmentation of α,β-epoxy-ketones upon treatment with a sulphonylhydrazine appeared to offer an attractive starting point for an alternative approach.[2,3] Thus, 17β-acetoxy-4ξ,5ξ-epoxyandrostan-3-one (1) in acetic acid–dichloromethane reacted with *p*-tolylsulphonylhydrazine at or below room temperature to give cleanly the 4,5-seco-derivative (3).[2a] Similar treatment of the 17β-hydroxy-epoxy-ketone (2)[4] afforded the expected product (4) (79%), and also two minor, less polar products. With prolonged reaction time the amounts of these other two products increased dramatically. They were identified as the 17-acetate (3) and the 17-toluene-*p*-sulphinate (5). An authentic sample of the latter was prepared by reaction of the alcohol (4) with toluene-*p*-sulphinyl chloride. The product, a mixture of epimers at sulphur, was crystallised to afford a pure sample of one isomer, m.p. 134—136 °C, $[\alpha]_D$ −76°. The o.r.d. spectrum of this isomer showed the first extremum of a negative Cotton effect at 276 nm, indicative of an *S*-configuration at sulphur.[5] The genesis of the products (3) and (5) must be related to the liberation of toluene-*p*-sulphinic acid in the fragmentation process. In accord with this, treatment of a solution of testosterone (6) in acetic acid–dichloromethane with toluene-*p*-sulphinic acid induced slow formation of the corresponding acetate (7) and toluene-*p*-sulphinate (8). In the absence of acetic acid, formation of the toluene-*p*-sulphinate was still observed. Similar results were obtained using other alcohols.[6] We believe that the active sulphinylating species in these interesting reactions is *p*-tolyl toluene-*p*-sulphinyl sulphone, a known intermediate in the decomposition of toluene-*p*-sulphinic acid.[7] Indeed, in subsequent work we have established that the sulphinyl sulphone is an extremely efficient and convenient sulphinylating agent.[8] We have not sought to establish the exact nature of the acetylating species, but a mixed anhydride[9] seems the most reasonable candidate for this role.



(1) R = Ac
(2) R = H

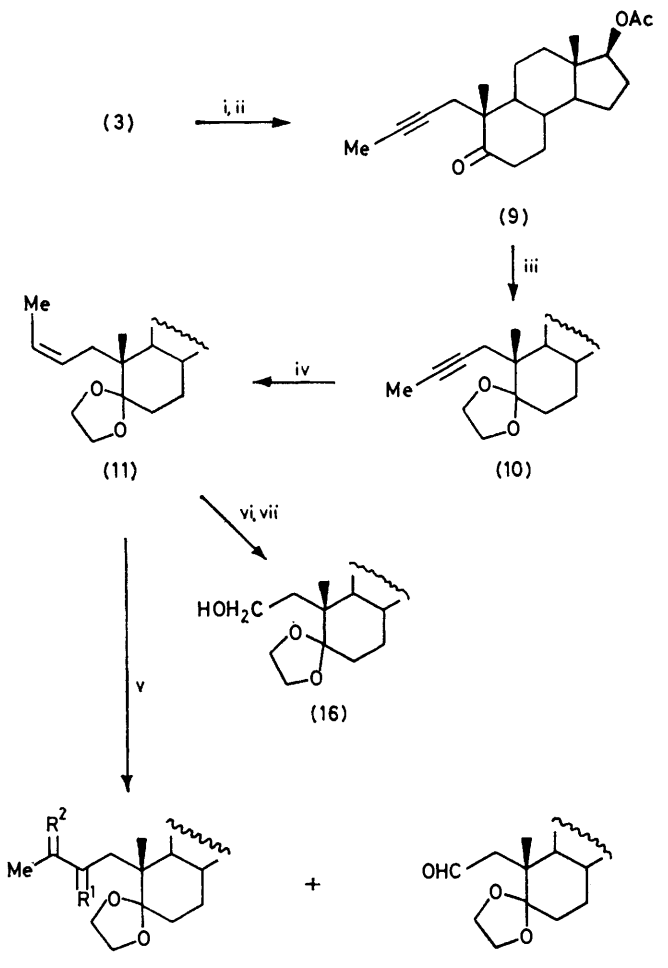


(3) R = Ac
(4) R = H
(5) R = S(O)-*p*-tolyl

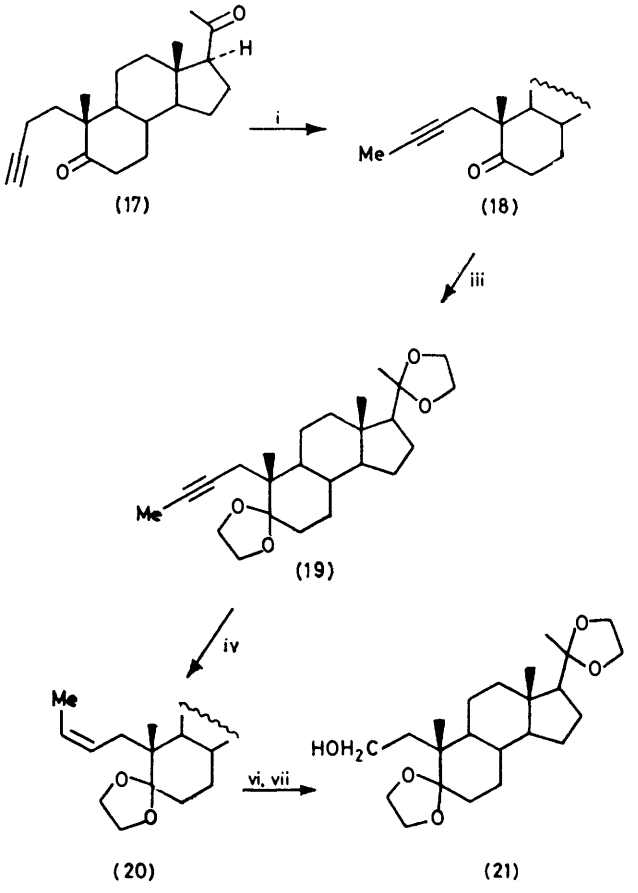


(6) R = H
(7) R = Ac
(8) R = S(O)-*p*-tolyl

Treatment of the terminal alkyne (3) with potassium t-butoxide in t-butyl alcohol gave, after reacetylation, the rearranged alkyne (9) in excellent yield. This reaction was conveniently followed by t.l.c. on silica gel impregnated with silver nitrate, the terminal alkyne remaining at the base line. The alk-2-yne (9) was converted into the corresponding acetal (10), which was hydrogenated over palladium–barium sulphate to afford the *Z*-alkene (11). Surprisingly, attempted cleavage of the alkene (11) by osmium tetraoxide and sodium periodate did not proceed satisfactorily. The expected aldehyde (12) was persistently accompanied by significant amounts of the 2,3-dione (13) and the α-hydroxy-ketones (14) and (15). However, the alkene (11) reacted cleanly with ozone to give, after work-up with sodium borohydride, the required alcohol (16) in 92% yield. Alternatively, work-up with dimethyl sulphide afforded a lower yield of the aldehyde (12). The overall yield of the dinor-alcohol (16) from the alkyne (3) was 62% (Scheme 1).



SCHEME 1 *Reagents*: i, KBu^{t}O, Bu^{t}OH; ii, Ac_2O, pyridine; iii, $HOCH_2CH_2OH$, TsOH; iv, H_2, Pd–$BaSO_4$; v, OsO_4, $NaIO_4$; vi, O_3; vii $NaBH_4$



SCHEME 2 *Reagents*: as in Scheme 1

In an analogous series of experiments, 4,5-secopregn-3-yne-5,20-dione (17) [2a] was converted into the dinor-alcohol (21) *via* intermediates (18)—(20) (Scheme 2).

The above sequence constitutes a short and efficient method for the removal of two carbon atoms from readily available [2,3] acetylenic ketones such as (3).

EXPERIMENTAL

M.p.s were determined for samples in open capillary tubes. N.m.r. data are for deuteriochloroform solutions with tetramethylsilane as internal reference and were recorded at 90 MHz unless otherwise stated. Rotations are of solutions in chloroform. I.r. data are for Nujol mulls. Light petroleum refers to the fraction of b.p. 60—80 °C.

Reaction of 17β-*Hydroxy*-4ξ,5ξ-*epoxyandrostan*-3-*one* (2) *with* p-*Tolylsulphonylhydrazine*.—17β-Hydroxy-4ξ,5ξ-epoxyandrostan-3-one [4] (3.73 g) in acetic acid (17 ml) and dichloromethane (17 ml) was cooled to −18 °C and *p*-tolylsulphonylhydrazine (2.75 g) was added. The yellow solution was stored at − 18 °C overnight and then allowed to warm to room temperature. After 4 h nitrogen evolution was complete. The now colourless solution was diluted with ether (60 ml) and washed with water, aqueous sodium hydrogen carbonate, and saturated aqueous sodium chloride, then dried and evaporated. The oily residue was chromatographed on a dry silica column (elution with 20% ethyl acetate in light petroleum) to afford 17β-acetoxy-4,5-secoandrost-3-yn-5-one (3) (55 mg), m.p. 94—97°, $[\alpha]_D$ +22° (*c* 0.5) (lit.,[2a] m.p. 95—96°, $[\alpha]_D$ +21°), a mixture of the 17β-acetate (3) and the 17β-toluene-*p*-sulphinate (5) (70 mg), and 17β-hydroxy-4,5-secoandrost-3-yn-5-one (2.8 g, 79%), an oil, $\nu_{max.}$ (neat) 3 460br, 3 300, 2 120, and 1 700 cm^{-1}; δ 0.83 and 1.11 (each 3 H, s, 18- and 19-H_3, respectively), and 3.67 (1 H, t, 17α-H); *m/z* 236 (100%) ($M^+ - C_4H_4$), 221 (28%), and 218 (15%).

The above experiment was repeated except that the reaction mixture was left at room temperature for an additional 24 h before work-up. The 17β-acetate (3), the 17β-toluene-*p*-sulphinate (5), and the 17β-alcohol (4) were obtained in the ratio 2 : 1 : 2.

Reaction of 17β-*Hydroxy*-4,5-*secoandrost*-3-*yn*-5-*one* (4) *with Toluene*-p-*sulphinyl Chloride*.—17β-Hydroxy-4,5-secoandrost-3-yn-5-one (500 mg) in pyridine (5 ml) was treated with toluene-*p*-sulphinyl chloride (465 mg). After 5 h at room temperature the mixture was poured into water and extracted with ether. The extracts were washed with 2M-hydrochloric acid, aqueous 2M-sodium carbonate, and saturated aqueous sodium chloride, dried, and evaporated.

The oily residue was treated with 20% ethyl acetate in light petroleum: a single isomer of the 17β-*toluene*-p-*sulphinate* (5) separated (160 mg, 22%), m.p. 134—136°, $[\alpha]_D$ −76° (*c* 0.67); $\nu_{max.}$ 3 295, 2 095, 1 710, 1 590, and 1 130 cm^{-1}; δ 0.84, 1.08, and 2.42 (each 3 H, s, 18- and 19-H_3 and Ar-CH_3, respectively), 4.16 (1 H, t, 17α-H), and 7.32 and 7.61 (each 2 H, d, *J* 9 Hz, Ar-H), *m/z* 374 (20%) (M^+-C_4H_4) and 271 (100%) (M^+-$ArSO_2$) (Found: C, 73.2; H, 8.0; S, 7.25. $C_{26}H_{34}SO_3$ requires C, 73.2; H, 8.0; S, 7.5%). Chromatography of the mother-liquors on a dry silica column gave *S*-*p*-tolyl toluene-*p*-thiosulphonate (50 mg), m.p. 76—78° (lit.,[10] 76—77°), and a solid (348 mg, 47%), evidently a mixture of diastereoisomers of the 17β-toluene-*p*-sulphinate (5), m.p. 98—102°, $[\alpha]_D$ +27° (*c* 0.64), δ 0.84 and 2.42 (each 3 H, s, 18-H_3 and Ar-CH_3), 1.06 and 1.08 (total 3 H, each s, 19-H_3), and 4.07 and 4.16 (total 1 H, each t, *J* 9 Hz, 17α-H).

Similarly, 17β-hydroxyandrost-4-en-3-one (testosterone) (6) afforded *S*-*p*-tolyl toluene-*p*-thiosulphonate and the 17β-*toluene*-p-*sulphinate* (8) (84%), m.p. (from chloroform–methanol) 169–175°, $[\alpha]_D$ +42° (*c* 0.77), $\nu_{max.}$ 1 665, 1 620, and 1 130 cm^{-1}, δ 0.84, 1.18, and 2.43 (each 3 H, s, 18- and 19-H_3 and Ar-CH_3 respectively), 4.14 (1 H, m, 17α-H), 5.74 (1 H, s, 4-H), and 7.34 and 7.61 (each 2 H, d, *J* 9 Hz, Ar-H) (Found: C, 73.2; H, 8.1; S, 7.55. $C_{26}H_{34}O_3S$ requires C, 73.2; H, 8.0; S, 7.5%).

Reactions of Testosterone (6) *with Toluene*-p-*sulphinic Acid*.—(*a*) Testosterone (100 mg) in acetic acid (1 ml) and dichloromethane (1 ml) was treated with toluene-*p*-sulphinic acid (108 mg). After 24 h at room temperature the mixture was poured into water and extracted with ether. The oily product was chromatographed on silica to afford *S*-*p*-tolyl toluene-*p*-thiosulphonate (20 mg), testosterone acetate (7), [68 mg, 60% (89% allowing for recovered starting material)], m.p. and mixed m.p. with an authentic sample 138—141°, testosterone toluene-*p*-sulphinate (8) (10 mg), identical with an authentic sample prepared above, and testosterone (31 mg).

(*b*) Similarly, testosterone (100 mg) in dichloromethane (3 ml) with toluene-*p*-sulphinic acid (270 mg) gave *S*-*p*-tolyl toluene-*p*-thiosulphonate (40 mg), testosterone toluene-*p*-sulphinate (8) [68 mg, 46% (76% allowing for recovered starting material)], and testosterone (40 mg).

17β-*Acetoxy*-4,5-*secoandrost*-2-*yn*-5-*one* (9).—17β-Acetoxy-4,5-secoandrost-3-yn-5-one (500 mg) in 4% potassium t-butoxide in t-butyl alcohol (15 ml) under nitrogen was heated under reflux for 2 h. The mixture was poured into water and extracted with ether. The oily product was treated with acetic anhydride in pyridine at room temperature overnight to afford the *acetate* (9) (442 mg, 88%), m.p. (from ethanol) 125—126°, $[\alpha]_D$ +72° (*c* 1.25); $\nu_{max.}$ 1 740 and 1 705 cm^{-1}; δ(200 MHz) 0.86, 1.07, and 2.05 (each 3 H, s, 18- and 19-H_3 and OAc, respectively), 1.74 (3 H, t, *J* 2.4 Hz, 4-H_3), 2.07 and 2.66 (each 1 H, dq, *J* 16 and 2.4 Hz, 1-H_2), and 4.65 (1 H, t, *J* 7.5 Hz, 17α-H), δ[($^2H_5$)pyridine] 0.83, 0.99, and 1.99 (each 3 H, s, 18- and 19-H_3 and OAc, respectively), 1.80 (3 H, t, *J* 2.5 Hz, 4-H_3), 2.12 and 2.83 (each 1 H, dq, *J* 16 and 2.5 Hz, 1-H_2), and 4.69 (1 H, t, *J* 7.5 Hz, 17α-H); *m/z* 330 (M^+) (Found: C, 76.3; H, 9.15. $C_{21}H_{30}O_3$ requires C, 76.3; H, 9.15%).

4,5-*Secopregn*-2-*yne*-5,20-*dione* (18).—4,5-Secopregn-3-yne-5,20-dione[2a] (1 g) in 4% potassium t-butoxide in t-butyl alcohol (50 ml) under nitrogen was heated under reflux for 3 h. The mixture was poured into water and extracted with ether to afford an oily product which was chromatographed on silica to give 4,5-*secopregn*-2-*yne*-5,20-*dione* (650 mg, 65%), m.p. (from ethyl acetate–light petroleum) 106—108°, $[\alpha]_D$ +159° (*c* 0.3); δ 0.68, 1.06, and 2.13 (each 3 H, s, 18-, 19-, and 21-H_3, respectively) and 1.73 (3 H, t, *J* 2 Hz, 4-H_3); *m/z* 314 (83%) (M^+), 299 (36%), 134 (43%), and 121 (100%) (Found: C, 80.0; H, 9.6. $C_{21}H_{30}O_2$ requires C, 80.25; H, 9.55%).

5,5-*Ethylenedioxy*-4,5-*secoandrost*-2-*yn*-17β-*yl Acetate* (10).—17β-Acetoxy-4,5-secoandrost-2-yn-5-one (450 mg), toluene-*p*-sulphonic acid (20 mg), and ethane-1,2-diol (4 ml) in benzene (35 ml) were heated under reflux with water separation for 3.5 h. The mixture was washed with aqueous 5% sodium hydrogen carbonate and saturated aqueous sodium chloride, then dried, and evaporated. The oily residue was chromatographed on a dry silica column. Elution with 10% ethyl acetate in light petroleum gave the *acetal* (10) (455 mg, 90%), m.p. (from chloroform–methanol) 74—76°, $[\alpha]_D$ +3° (*c* 0.87), δ 0.77, 1.01, and 2.00 (each 3 H, s, 18- and 19-H_3 and OAc, respectively), 1.75 (3 H, t, *J* 2.5 Hz, 4-H_3), 2.17 (2 H, t, *J* 2.5 Hz, 1-H_2), 3.92 (4 H, s, OCH_2-CH_2O), and 4.59 (1 H, t, *J* 7.5 Hz, 17α-H); *m/z* 374 (9%) (M^+) and 99 (100%) (Found: C, 73.6; H, 9.3. $C_{23}H_{34}O_4$ requires C, 73.8; H, 9.15%).

Similar treatment of 4,5-secopregn-2-yne-5,20-dione (18) under reflux for 48 h afforded 5,5;20,20-*bis*(*ethylenedioxy*)-4,5-*secopregn*-2-*yne* (19) (70%), m.p. (from pentane) 109—111°, $[\alpha]_D$ +24° (*c* 0.8); δ 0.76, 1.02, and 1.28 (each 3 H, s, 18-, 19-, and 21-H_3, respectively), 1.74 (3 H, t, *J* 2 Hz, 4-H_3), and 3.94 br (8 H, s, 2 × OCH_2CH_2O); *m/z* 402 (6%) (M^+) and 99 (100%) (Found: C, 74.8; H, 9.5. $C_{25}H_{38}O_4$ requires C, 74.6; H, 9.5%).

(Z)-5,5-*Ethylenedioxy*-4,5-*secoandrost*-2-*en*-17β-*yl Acetate* (11).—5,5-Ethylenedioxy-4,5-secoandrost-2-yn-17β-yl acetate (2.8 g) in hexane (50 ml) was shaken under hydrogen with 10% palladium–barium sulphate (100 mg). When 1 equiv. of hydrogen had been taken up (*ca.* 1 h), the catalyst was filtered off and the filtrate was evaporated to dryness. Crystallisation of the residue from ethanol gave the *alkene* (2.0 g), m.p. 95—96°, $[\alpha]_D$ +12° (*c* 0.68); $\nu_{max.}$ 3 030 and 1 745 cm^{-1}; δ 0.79, 1.02, and 2.02 (each 3 H, s, 18- and 19-H_3 and OAc, respectively), 3.88 (4 H, s, OCH_2CH_2O), 4.58 (1 H, t, *J* 7.5 Hz, 17α-H), and 5.2—5.9 (2 H, m, 2- and 3-H); *m/z* 376 (2%) (M^+) and 99 (100%) (Found: C, 73.2; H, 9.65. $C_{23}H_{36}O_4$ requires C, 73.4; H, 9.6%).

The mother-liquors were evaporated and the residue was chromatographed on a dry silica column (elution with 10% ethyl acetate in light petroleum). This afforded 5,5-ethylenedioxy-4,5-secoandrostan-17β-yl acetate as an oil which slowly crystallised, m.p. 90—93°, $[\alpha]_D$ +22° (*c* 0.92); δ 0.79, 0.96, and 2.02 (each 3 H, s, 18- and 19-H_3 and OAc, respectively), 3.9 (4 H, s, OCH_2CH_2O), and 4.60 (1 H, t, 17α-H); *m/z* 378 (2%) (M^+) and 99 (100%); followed by further alkene (11) (380 mg, total yield 85%).

5,5;20,20-Bis(ethylenedioxy)-4,5-secopregn-2-yne (19) was similarly hydrogenated. Chromatography on silica gave 5,5;20,20-bis(ethylenedioxy)-4,5-secopregnane as an oil which slowly crystallised, m.p. 69—71°, $[\alpha]_D$ +37° (*c* 0.67); δ 0.76, 0.94, and 1.28 (each 3 H, s, 18-, 19-, and 21-H_3, respectively), and 3.90br (8 H, s, 2 × OCH_2CH_2O); *m/z* 406 (3%) (M^+) and 99 (100%); followed by 5,5;20,20-*bis*(*ethylenedioxy*)-4,5-*secopregn*-2-*ene* (75%), m.p. (from pentane) 66—68°, $[\alpha]_D$ +46° (*c* 0.8); $\nu_{max.}$ 1 650 cm^{-1}; δ 0.78, 1.03, and 1.21 (each 3 H, s, 18-, 19-, and 21-H_3), 3.90br (8 H, s, 2 × OCH_2CH_2O), and 5.2—5.9 (2 H, m, 2- and 3-H); *m/z* 404 (2%) (Found: C, 74.35; H, 9.9. $C_{25}H_{40}O_4$ requires C, 74.2; H, 10.0%).

Treatment of (Z)-5,5-*Ethylenedioxy*-4,5-*secoandrost*-2-*en*-17β-*yl Acetate with Osmium Tetraoxide and Sodium Periodate.*—The alkene (200 mg) in dioxan (10 ml) at room temperature was treated with osmium tetraoxide (20 mg) in dioxan (2 ml). The mixture developed a dark brown colour almost immediately. After 45 min, water (1 ml) was added followed dropwise over 3 h by sodium periodate (250 mg) in water (4 ml). The colour of the mixture was gradually discharged and a white precipitate formed. The mixture was poured into water and extracted with ether to afford a black oil. Chromatography on a dry silica column (elution with 20—60% ethyl acetate in light petroleum) gave 17β-*acetoxy*-5,5-*ethylenedioxy*-2,5-*seco*-3,4-*dinorandrostan*-2-*al* (12) (97 mg, 50%), m.p. (from ethanol) 153—156°, $[\alpha]_D$ +27° (*c* 0.9); $\nu_{max.}$ 2 760, 1 740, 1 710, and 1 240 cm^{-1}; δ 0.82, 1.20, and 2.02 (each 3 H, s, 18- and 19-H_3 and OAc, respectively), 2.23 (2 H, d, *J* 4 Hz, 1-H_2), 3.65—3.93 (4 H, m, OCH_2CH_2O), 4.58 (1 H, t, *J* 9 Hz, 17α-H), and 9.68 (1 H, t, *J* 4 Hz, 2-H); *m/z* 364 (1%) (M^+) and 99 (100%) (Found: C, 69.2; H, 8.8. $C_{21}H_{32}O_5$ requires C, 69.2; H, 8.85%); followed by 17β-*acetoxy*-5,5-*ethylenedioxy*-4,5-*secoandrostane*-2,3-*dione* (13), m.p. (from ethanol) 94—96°, $[\alpha]_D$ +44° (*c* 0.7); $\nu_{max.}$ 1 735br and 1 700 cm^{-1}; δ 0.81, 1.11, and 2.03 (each 3 H, s, 18- and 19-H_3 and OAc, respectively), 2.20 and 3.13 (each 1 H, d, *J* 14 Hz, 1-H_2), 2.28 (3 H, s, 4-H_3), 3.6—3.9 (4 H, m, OCH_2CH_2O), and 4.60 (1 H, t, *J* 9 Hz, 17α-H); *m/z* 406 (3%) (M^+), 363 (21%) ($M^+ - CH_3CO$), and 99 (100%) (Found: C, 68.2; H, 8.5. $C_{23}H_{34}O_6$ requires C, 67.95; H, 8.4%); followed by a mixture of 17β-acetoxy-5,5-ethylenedioxy-3ξ-hydroxy-4,5-secoandrostan-2-one (14) and 17β-acetoxy-5,5-ethylenedioxy-2ξ-hydroxy-4,5-secoandrostan-3-one (15), m.p. (from ethanol) 168—174°, $[\alpha]_D$ +79° (*c* 0.3); $\nu_{max.}$ 3 480, 1 725, 1 710, and 1 245 cm^{-1}; *m/z* 408 (8%) (M^+) and 99 (100%) (Found: C, 67.5; H, 8.8. $C_{23}H_{36}O_6$ requires C, 67.6; H, 8.9%).

5,5-*Ethylenedioxy*-2,5-*seco*-3,4-*dinorandrostane*-2,17β-*diol* 17-*Acetate* (16).—(*Z*)-5,5-Ethylenedioxy-4,5-secoandrost-2-en-17β-yl acetate (685 mg) in methanol (70 ml) at −70 °C was treated with a stream of ozone until no starting material remained (30 min). The solution was purged with nitrogen and allowed to warm to room temperature, and sodium borohydride (500 mg) was added. After 15 min the solution was evaporated to half volume, diluted with water, and extracted with ether to give the *alcohol* (16) (613 mg, 92%), m.p. (from light petroleum) 145—148°, $[\alpha]_D$ +26° (*c* 0.7); δ 0.81, 1.04, and 2.02 (each 3 H, s, 18- and 19-H_3 and OAc, respectively), 3.5—3.8 (2 H, m, 2-H_2), 3.96 (4 H, s, OCH_2CH_2O), and 4.59 (1 H, t, *J* 9 Hz. 17α-H); *m/z* 366 (1%) (M^+) and 99 (100%) (Found: C, 68.6; H, 9.05. $C_{21}H_{34}O_5$ requires C, 68.8; H, 9.35%).

The above experiment was repeated except that the ozonised solution was treated with dimethyl sulphide instead of sodium borohydride. Work-up and chromatography then gave 17β-acetoxy-5,5-ethylenedioxy-2,5-seco-3,4-dinorandrostan-2-al (12) (45%), identical with the material described above.

Similar ozonolysis of 5,5-ethylenedioxy-4,5-secoandrost-2-yn-17β-yl acetate (10) and work-up with dimethyl sulphide afforded (after chromatography) starting material and 17β-acetoxy-5,5-ethylenedioxy-4,5-secoandrostane-2,3-dione (13), identical with the material described above.

Similar ozonolysis of 5,5;20,20-bis(ethylenedioxy)-4,5-secopregn-2-ene and work-up with sodium borohydride gave 5,5;20,20-*bis*(*ethylenedioxy*)-2,5-*seco*-2,4-*dinorpregnan*-2-*ol* (21) (70%), m.p. (from ethyl acetate–light petroleum) 170—171°, $[\alpha]_D$ +37° (*c* 0.6); δ 0.78, 1.04, and 1.29 (each 3 H, s, 18-, 19-, and 21-H_3, respectively), and 3.5—4.1 (10 H, m, 2-H_2 and 2 × OCH_2CH_2O); *m/z* 394 (1%) (M^+), 99 (34%), and 87 (100%) (Found: C, 70.4; H, 9.7. $C_{23}H_{38}O_5$ requires C, 70.0; H, 9.7%).

We thank the S.R.C. for financial support and G. D. Searle Ltd., High Wycombe for participation in a CASE award.

[1/1184 *Received*, 27*th July*, 1981]

REFERENCES

[1] See, for example, F. L. Weisenborn, D. C. Remy, and T. L. Jacobs, *J. Am. Chem. Soc.*, 1954, **76**, 552; J. T. Edward, D. Holder, W. H. Lunn, and I. Puskas, *Can. J. Chem.*, 1961, **39**, 599; D. J. Hampson, G. D. Meakins, and D. J. Morris, *J. Chem Soc. C*, 1966, 1277; R. Heckendorn and C. Tamm, *Helv. Chim. Acta*, 1967, **50**, 1499; D. M. Piatak, H. B. Bhat, and E. Caspi, *J. Org. Chem.*, 1969, **34**, 112.

[2] (*a*) J. Schreiber, D. Felix, A. Eschenmoser, M. Winter, F. Gautschi, K. H. Schulte-Elte, E. Sundt, G. Ohloff, J. Kalvoda, H. Kaufmann, P. Wieland, and G. Anner, *Helv. Chim. Acta*, 1967, **50**, 2101; (*b*) M. Tanabe, D. F. Crowe, R. L. Dehn, and G. Detre, *Tetrahedron Lett.*, 1967, 3739; M. Tanabe, D. F. Crowe, and R. L. Dehn, *ibid.*, 1967, 3943; (*c*) C. B. Reese and H. P. Sanders, *Synthesis*, 1981, 276.

[3] For related reactions see, G. A. MacAlpine and J. Warkentin, *Can. J. Chem.*, 1978, **56**, 308 and references therein; C. Fehr, G. Ohloff, and G. Buchi, *Helv. Chim. Acta*, 1979, **62**, 2655.

[4] H. J. Ringold, E. Batres, O. Mancera, and G. Rosenkranz, *J. Org. Chem.*, 1956, **21**, 1432; B. Camerino, B. Patelli, and A. Vercellone, *J. Am. Chem. Soc.*, 1956, **78**, 3540.

[5] K. Mislow, M. M. Green, P. Laur, J. T. Melillo, T. Simmons, and A. L. Ternay, *J. Am. Chem. Soc.*, 1965, **87**, 1958.

[6] R. B. Boar and A. C. Patel, unpublished observations.

[7] H. Bredereck, A. Wagner, H. Beck, and R.-J. Klein, *Chem. Ber.*, 1960, **93**, 2736; J. L. Kice, G. Guaraldi, and C. G. Venier, *J. Org. Chem.*, 1966, **31**, 3561.

[8] R. B. Boar and A. C. Patel, in preparation.

[9] M. Kobayashi, *Bull. Chem. Soc. Jpn.*, 1966, **39**, 967.

[10] M. Furukawa, T. Okawara, Y. Noguchi, and M. Nishikawa, *Synthesis*, 1978, 441.