Acid-Catalysed Cleavage of Some 3-Substituted 5α,6α-Epoxy-7-Norandrostan-17-ones

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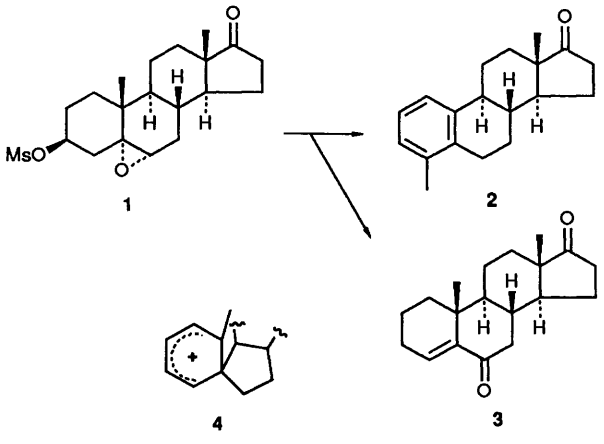
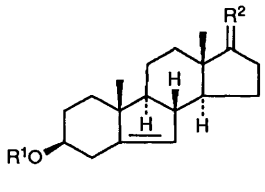
Crystallographic and spectroscopic studies show that treatment of 3β-acetoxy-5α,6α-epoxy-7-norandrostan-17-one with HBr in glacial acetic acid gives 3β-acetoxy-6-bromo and 3β,6-dibromo-7-norandrost-5-en-17-one and 5β-bromo-3α,6α-epoxy-7-norandrostan-17-one. Cleavage of the epoxide with periodic acid gives the 5β,6α-diol. The corresponding 3β-methanesulphonate gave 3β,6β-dibromo-5β-methyl-7,19-dinorandrost-9-en-17-one and 1-methyl-7-norestra-1,3,5(10)-trien-17-one. The formation of these products is rationalized in terms of the various modes of collapse of a C-5 carbocation.

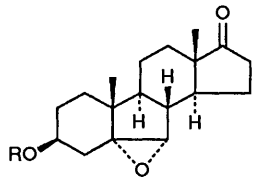
The acid-catalysed aromatization of ring A of steroids containing three double-bond equivalents on rings A or B is a well known rearrangement.[1,2] This reaction leads to oestra-1,3,5(10)-trienes in which the original C-10 methyl group is eventually located at either C-1 or C-4. There are a number of other competing reactions which may accompany the aromatization. Treatment of 3β-methylsulphonyloxy-5α,6α-epoxyandrostan-17-one **1** with hydrogen bromide in acetic acid affords 4-methylestra-1,3,5(10)-trien-17-one **2** and androst-4-ene-6,17-dione **3**.[3] In this case the formation of the 4-methylestra-1,3,5(10)-triene follows the dienol:benzene pathway and involves the spiranic intermediate **4**. This intermediate would become a highly strained system in the corresponding B-norsteroid series. We have therefore examined the acid-catalysed rearrangement of some epoxides in the B-norsteroid series to see what reactions occur with the constraints imposed by a five-membered ring. The reaction of 5α,6α-epoxy-7-norsteroids with either boron trifluoride or acetic acid have been examined previously[4,5] and shown to give 'backbone' rearrangement products. Under these conditions, no aromatic products were detected. Our results, which extend and differ in detail from those of the previous workers, form the subject of this paper.



Treatment of 3β-acetoxy-7-norandrost-5-en-17-one **5** with *m*-chloroperbenzoic acid (MCPBA) gave the known 5α,6α-epoxide **9**.[5] In the previous work the stereochemistry of the epoxide was assigned from the ease with which it underwent the C-10–C-5 methyl-group migration. Further evidence was obtained by reduction of the epoxide with lithium aluminium hydride. This has been reported to give either a C-5[5] or a C-6 alcohol.[4] In our hands this reaction gave two products. The first was the known triol **11**,[5] which was acetylated with acetic anhydride in pyridine to give 3β,17β-diacetoxy-5α-hydroxy-7-norandrostane **12**. The 3-H NMR resonance (δ 4.97) appeared as a triplet (*J* 11.2 Hz) of triplets (*J* 5.1 Hz). This multiplicity indicated that it was an axial proton and hence there was a *trans* A/B ring junction. Furthermore, this resonance experienced a solvent-induced shift ($\Delta_{C_5D_5N} - \Delta_{CDCl_3}$) of 0.24 ppm, indicating that this proton has a diaxial relationship to a 5α-hydroxy group. Hence the original epoxide had the 5α,6α-stereochemistry. The second product of the lithium aluminium hydride reduction was an unstable gum, which on further chromatography decomposed to give 3β,17β-dihydroxy-7-norandrost-5-ene **7**. It is possible that the original gum was a triol.

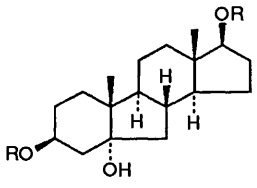


5 R^1 = Ac, R^2 = O
6 R^1 = Ms, R^2 = O
7 R^1 = H, R^2 = α-H, β-OH
8 R^1 = H, R^2 = O

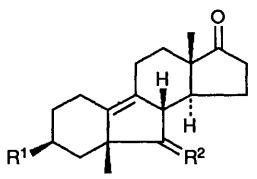


9 R = Ac
10 R = Ms

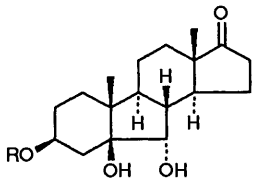
Treatment of the 3β-acetoxy-5α,6α-epoxy-7-norandrostan-17-one **9** with boron trifluoride–diethyl ether led to the known 9-ene **13**[5] which was formed by a 'backbone' rearrangement. The ^{1}H NMR spectrum was consistent with the previously proposed structure. In particular, the 3-H NMR signal (δ 5.18) was a narrow pentuplet (*J* 3 Hz), consistent with this H-atom being an equatorial proton and thus with the presence of a C-5 methyl substituent. The C-6 proton signal was a doublet (δ 3.74, *J* 5 Hz). Treatment of the epoxide with refluxing acetic acid gave the same compound **13**, together with a gummy acetate which was not described in the previous work. This acetate was hydrolysed (base) to a crystalline triol. The triol was assigned the structure **16** on the basis of the following evidence. The C-3 proton resonance in compound **16** (δ 4.21) was a pentuplet, *J* 3 Hz. The signal was therefore due to an equatorial proton consistent with an inversion of configuration at C-5. The C-6 proton resonance was a doublet, 3.99 (*J* 8.1 Hz), which was coupled to the C-8 proton signal (δ 2.05). Irradiation of both the methyl signals (δ 0.91 and 0.92)



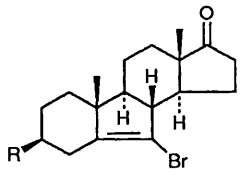
11 R = H
12 R = Ac



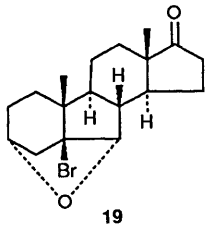
13 R^1 = OAc, R^2 = α-OH, β-H
14 R^1 = Br, R^2 = α-H, β-Br



15 R = Ac
16 R = H



17 R = Br
18 R = OAc



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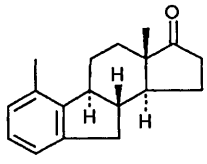

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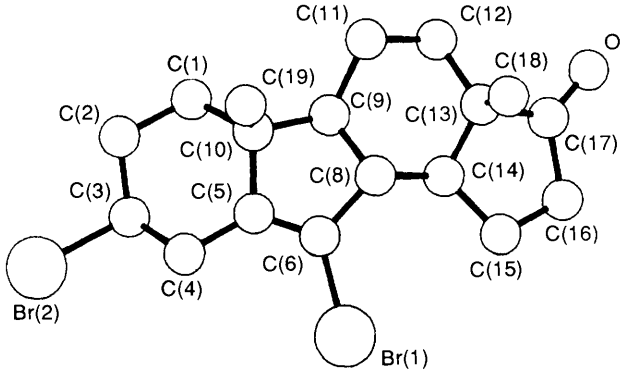


Fig. 1 X-Ray molecular structure of 3β,6-dibromo-7-norandrost-5-en-17-one **17**

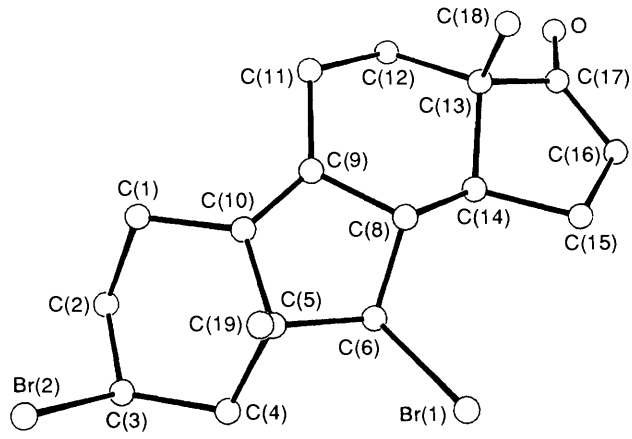


Fig. 2 X-Ray molecular structure of 3β,6β-dibromo-5β-methyl-7,19-dinorandrostan-17-one **14**

produced NOE enhancements (10 and 8%, respectively) of this signal. Irradiation of the signal at δ 0.92 also produced an enhancement of the C-6 proton signal at δ 3.99 and hence the latter must have the β-configuration. This leads to the overall structure **16** for the triol. Cleavage of the epoxide with chromium trioxide or, better, with periodic acid gave the 5β,6α-diol **15** without any rearrangement products.

When the cleavage of the epoxide was carried out with hydrogen bromide in glacial acetic acid, three compounds were obtained. These were separated by chromatography. The least polar compound, $C_{18}H_{24}Br_2O$, was a bromo alkene, possessing the enhanced IR absorption (ν_{max} 1635 cm^{-1}) typical of a vinyl halide. It possessed alkene ^{13}C NMR signals at δ_C 117.65 and 146.53. There were no attached hydrogen atoms. There was only one C*H*(Br) signal (δ 3.88), the multiplicity of which (triplet, *J* 8 Hz, of triplets, *J* 4 Hz) showed that it was due to an axial proton at C-3. This is consistent with the structure **17** although it did not entirely exclude alternatives derived from a 'backbone' rearrangement. The structure was therefore confirmed by X-ray analysis (see Fig. 1).

The second compound was an ether, $C_{18}H_{25}BrO_2$. Its IR spectrum showed only the carbonyl absorption (ν_{max} 1747 cm^{-1}) which was assigned to the C-17 ketone. The ^1H NMR spectrum showed CH–O signals at δ 4.19 (doublet, *J* 2 Hz) and 4.32 (triplet, *J* 5.3 Hz). Selective population transfer studies showed that the signal at δ 4.19 was coupled to a broad triplet, δ 2.10, whilst that at 4.32 was coupled to signals at δ 2.4 and 1.7. The signal at δ 2.10 showed NOE enhancements (10 and 2%, respectively) on irradiation of each of the methyl signals (δ 0.92 and 1.11) and hence it was assigned to 8-H. These spectral data were consistent with the ether formulation **19**. Similar ethers have been described previously in the B-norsteroid series.[6]

The third compound, $C_{20}H_{27}BrO_3$, was clearly the 3β-acetate **18** corresponding to the dibromide **17**. In particular, it possessed a ^1H NMR signal at δ 4.65 which was a triplet (*J* 11.5 Hz) of triplets (*J* 4.5 Hz) and the ^{13}C NMR signals for the bromo alkene group at δ_C 145.54 and 118.13.

3β-Hydroxy-7-norandrost-5-en-17-one **8** was converted into its methanesulphonate, which was then epoxidized with MCPBA to form the 5α,6α-epoxide **10**. Treatment of this compound with hydrogen bromide in glacial acetic acid gave three products, which were separated by column chromatography. The least polar compound was a dibromide, $C_{18}H_{24}Br_2O$. The ^1H NMR spectrum contained two CH(Br) resonances, δ 3.63 (doublet, *J* 8.7 Hz) and 4.63 (pentuplet, *J* 3.6 Hz), whilst the ^{13}C NMR spectrum revealed the presence of a tetrasubstituted alkene, δ_C 138.88 and 131.98. This evidence was consistent with the overall formulation **14** but did not rigorously define the stereochemistry, particularly on ring B. This was then established by X-ray analysis (see Fig. 2). The second product was an isomeric dibromide which was identified as the bromo alkene **17**, which had been obtained previously from the 3β-acetate **9**. The third product, which was difficult to obtain pure and was sometimes crystallized as a monohydrate, was the aromatic steroid **20**. Its ^1H NMR spectrum possessed signals at δ 2.37 (Ar*Me*), 6.90 (doublet, *J* 7.5 Hz), 7.03 (triplet, *J* 7.5 Hz) and 7.08 (doublet, *J* 7.5 Hz). Its structure and stereochemistry, particularly that of the B/C ring junction, was confirmed by X-ray analysis (see Fig. 3).

Any scheme to accommodate these results must account for the substitution at C-3 by bromine with retention of configuration whilst the introduction of bromine at C-6 proceeds with inversion of configuration. On the other hand cleavage of the epoxide with periodic acid affords the 5β,6α-diol **15**. The key to this may lie in the isolation of the 3α,6α-ether **19**. This was shown to give 3β,6-dibromo-7-norandrost-5-en-17-one **17** on small-scale treatment with hydrogen bromide in

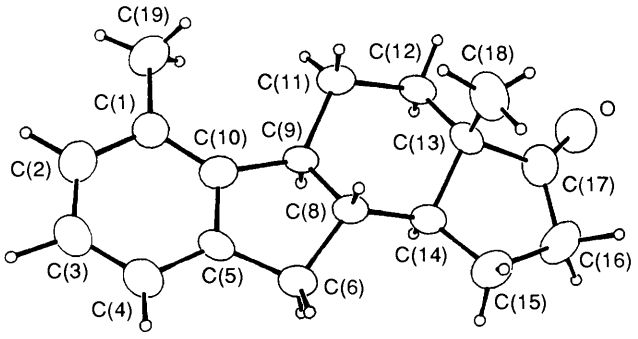
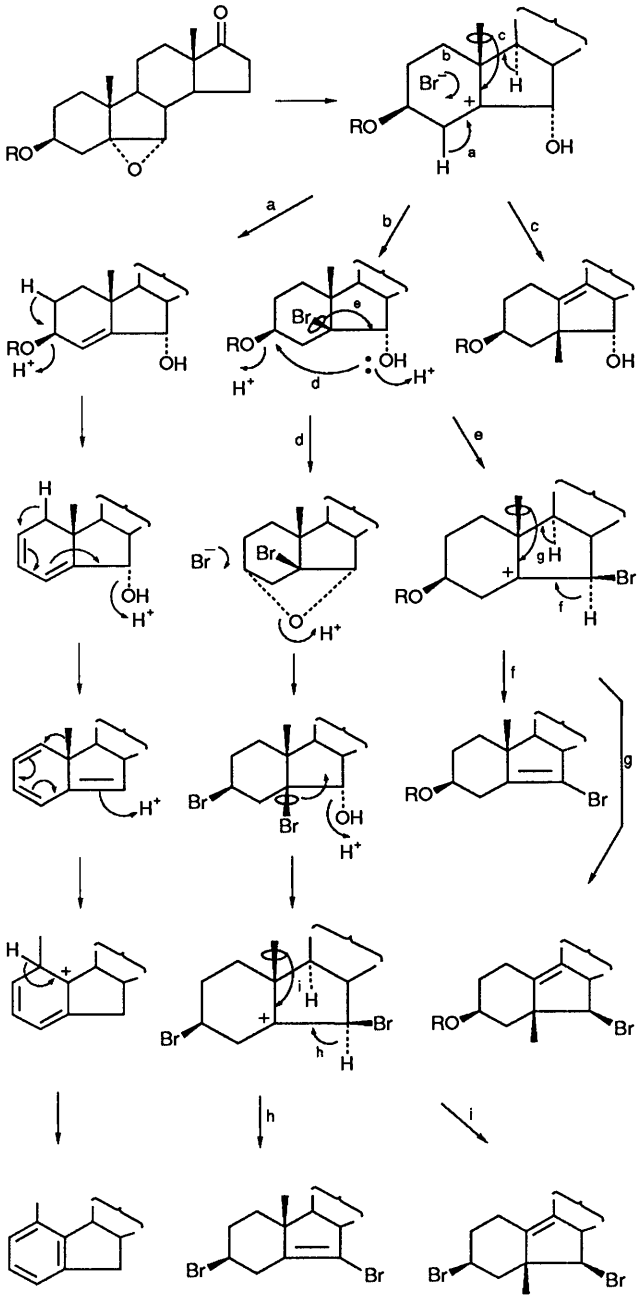


Fig. 3 X-Ray molecular structure of 1-methyl-7-norestra-1,3,5(10)-trien-17-one **20**



Scheme 1

glacial acetic acid. The reaction products may be accounted for by the various modes of decomposition of a C-5 carbocation. Thus loss of a proton from C-4 converts the C-3 substituent into an allylic derivative which may then undergo further elimination and eventual aromatization by a methyl migration to C-1 (see Scheme 1). On the other hand discharge of the C-5 carbocation by attack of bromine from the β-face produces a *cis* ring junction which permits ether formation between C-6 and C-3. The ether may, in turn, undergo acid-catalysed cleavage with rearrangement of the C-5 bromine atom to C-6. The hydrolysis of the 3α,6α-ether also leads to the introduction of a 3β-bromine atom. A third mode of discharge of the C-5 carbocation involves the migration of the methyl group from C-10 to C-5. The interplay of these steps may account for the formation of the wide range of products. In conclusion the acid-catalysed cleavage reactions of the 5α,6α-epoxides in the B-norsteroid series show very significant differences from those of the normal series brought about by the different geometry of the initial cleavage of the epoxide.

Experimental

General Experimental Details.—^{1}H and ^{13}C NMR spectra were determined at 360 and 90.55 MHz, respectively, on a Bruker WM 360 spectrometer. *J*-Values are given in Hz. IR spectra were determined as Nujol mulls on a PE 1710 spectrometer. Extracts were dried over sodium sulphate. Silica for chromatography was Merck 9385. Light petroleum refers to the fraction boiling in the range 60–80 °C. 3β-Acetoxy-7-norandrost-5-en-17-one was prepared according to the method of Knof[7,8] and had m.p. 137–138 °C (lit.,[8] 137–138 °C). The epoxide, prepared with MCPBA in chloroform, had m.p. 165–168 °C (lit.,[9] 165–167 °C).

Reduction of 3β-*Acetoxy*-5α,6α-*epoxy*-7-*norandrostan*-17-*one* **9**.—The epoxide (500 mg) was added to a suspension of lithium aluminium hydride (500 mg) in dry tetrahydrofuran (100 cm^3) and the mixture was heated under reflux under nitrogen for 24 h. The mixture was cooled, diluted with ethyl acetate and then acidified with dil. hydrochloric acid. The steroids were extracted with ethyl acetate. The extract was washed successively with aq. sodium hydrogen carbonate and water, and dried. The solvent was evaporated off to give a residue, which was chromatographed on silica. Elution with 20% ethyl acetate–light petroleum gave 7-norandrostane -3β,5α,17β-triol **11** (210 mg), which was crystallized from ethyl acetate–light petroleum as needles, m.p. 175–177 °C (lit.,[5] 174–176 °C) (Found: C, 72.9; H, 10.3. Calc. for $C_{18}H_{30}O_3$: C, 73.4; H, 10.3%); ν_{max}/cm^{-1} 3409; δ 0.73 (3 H, s, 18-H$_3$), 0.90 (3 H, s, 19-H$_3$), 3.69 (1 H, t, *J* 8, 17-H) and 3.94 [1 H, t, (*J* 10.9) of t (*J* 4.6), 3-H]. Further elution gave an unstable oil (100 mg) [δ(90 MHz) 0.73 and 0.87 (CMe) and 3.55–3.65 multiplets], which on further chromatography gave 7-*norandrost*-5-*ene*-3β,17β-*diol* **7**, m.p. 189–191 °C (Found: C, 75.0; H, 10.0. $C_{18}H_{28}O_2$·0.5 H_2O requires C, 75.2; H, 10.2%); ν_{max}/cm^{-1} 3200br; δ 0.77 (3 H, s, 18-H$_3$), 0.89 (3 H, s, 19-H$_3$), 3.58 [1 H, t, (*J* 11.5) of t (*J* 4.5), 3-H], 3.68 (1 H, t, *J* 7.3, 17-H) and 5.35 (1 H, br s, 6-H). 3β,17β-Diacetoxy-7-norandrostane-5α-ol **12**, prepared by reaction with acetic anhydride in pyridine, had m.p. 168–170 °C (lit.,[5] 169–170 °C) (Found: C, 70.4; H, 8.5. Calc. for $C_{22}H_{34}O_5$: C, 70.0; H, 9.0%); ν_{max}/cm^{-1} 3527 and 1735; δ 0.78 (3 H, s, 18-H$_3$), 0.91 (3 H, s, 19-H$_3$), 2.03 and 2.04 (each 3 H, s, OAc), 4.64 (1 H, t, *J* 7.5, 17-H) and 4.97 [1 H, t (*J* 11.2) of t (*J* 5.1), 3-H].

Reaction of 3β-*Acetoxy*-5α,6α-*epoxy*-7-*norandrostan*-17-*one* **9** *with Boron Trifluoride-Diethyl Ether.*—A solution of the epoxide (300 mg) in dry diethyl ether (5 cm^3) was treated with boron trifluoride–diethyl ether (5 cm^3) at 0 °C for 5 h. The mixture was diluted with diethyl ether, washed successively with aq. sodium hydrogen carbonate and water, and dried.

Table 1 Crystal data and structure refinement details for the X-ray structures

	17	**14**	**20**
Formula	$C_{18}H_{24}Br_2O$	$C_{18}H_{26}Br_2O$	$C_{18}H_{22}O$
M	416.2	418.2	254.4
Crystal size (mm)	0.2 × 0.2 × 0.1	0.5 × 0.1 × 0.05	0.3 × 0.3 × 0.3
Crystal system	orthorhombic	orthorhombic	monoclinic
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_1$
a, *b*, *c* (Å), β (°)	8.596(1), 11.972(2), 16.742(2), 90	6.589(2), 15.792(5), 17.255(4), 90	6.940(3), 7.291(6), 14.208(4), 101.32(3)
V (Å^3)	1721.4	1795.5	704.9
Z, D_c (g cm^{-3}), *F*(000)	4, 1.61, 840	4, 1.55, 848	2, 1.19, 276
μ Mo-*K*α (cm^{-1})	46.6	44.5	0.6
Total unique reflections	1772	1855	1383
Significant reflections $I > \sigma(I)$	1140	712	1088
Abs. corr. (max/min)	1.61, 0.61	none	none
Hydrogen atoms	fixed calculated	omitted	refined
R	0.035	0.074	0.060
R'	0.037	0.093	0.076
$\Delta\rho_{max}$ for final difference map (e Å^{-3})	0.3	0.8	0.7

Evaporation of the solvent gave 3β-acetoxy-6α-hydroxy-5β-methyl-7,19-dinorandrost-9-en-17-one **13** (285 mg), which was crystallized from aq. methanol as needles, m.p. 105–107 °C (lit.,[5] 99–101 °C) (Found: C, 68.3; H, 8.5. Calc. for $C_{20}H_{28}O_4 \cdot H_2O$: C, 68.5; H, 8.6%); ν_{max}/cm^{-1} 3403, 1732 and 1708; δ 0.89 (3 H, s, 18-H$_3$), 1.04 (3 H, s, 19-H$_3$), 2.02 (3 H, s, OAc), 3.73 (1 H, d, *J* 5, 6-H) and 5.18 (1 H, pentuplet, *J* 3, 3-H).

Reaction of 3β-*Acetoxy*-5α,6α-*epoxy*-7-*norandrostan*-17-*one* **9** *with Glacial Acetic Acid.*—The epoxide (500 mg) was heated with glacial acetic acid (5 cm^3) under reflux for 30 min. The solution was poured into cold, aq. sodium hydrogen carbonate and the steroids were recovered with ethyl acetate. The extract was washed with water and was then dried. The solvent was evaporated off to give a gum, which was chromatographed on silica. Elution with 20% ethyl acetate–light petroleum afforded a mixture (200 mg). Further elution afforded 3β-acetoxy-6α-hydroxy-5β-methyl-7,19-dinorandrost-9-en-17-one **13** (150 mg), identical (IR, NMR) with the material described above.

The mixture (200 mg) was dissolved in methanol (6 cm^3) and the solution was heated with aq. potassium hydroxide (600 mg in 1 cm^3) under reflux for 1 h. The solution was cooled, acidified with dil. hydrochloric acid, and the products were recovered in ethyl acetate. The extract was washed with aq. sodium hydrogen carbonate and dried. The solvent was evaporated off to afford 3β,5β,6α-*trihydroxy*-7-*norandrostan*-17-*one* **16** (100 mg), which was crystallized from ethyl acetate–light petroleum as cubes, m.p. 203–205 °C (Found: C, 68.5; H, 8.9. $C_{18}H_{26}O_4 \cdot 0.5\ H_2O$ requires C, 68.5; H, 8.6%), ν_{max}/cm^{-1} 3444 and 1734; δ 0.91 and 0.92 (each 3 H, s, together 18- and 19-H$_3$), 3.99 (1 H, d, *J* 8, 6-H) and 4.21 (1 H, pentuplet, *J* 3.6, 3-H).

Reaction of 3β-*Acetoxy*-5α,6α-*epoxy*-7-*norandrostan*-17-*one* **9** *with Chromium Trioxide.*—Aq. chromium trioxide (75%; 2.5 cm^3) was added dropwise to a stirred solution of the epoxide **9** (500 mg) in methyl ethyl ketone (10 cm^3) at 35–40 °C. The solution was left for 5 h and was then poured into water. The products were recovered in ethyl acetate and the extracts were washed thoroughly with water and dried. The solvent was evaporated off and the residue was chromatographed on silica. Elution with 15% ethyl acetate–light petroleum gave the starting material (420 mg recovery). Elution with 30% ethyl acetate–light petroleum gave 3β-acetoxy-5β,6α-dihydroxy-7-norandrostan-17-one **15** (40 mg), which was crystallized from ethyl acetate as needles, m.p. 173–176 °C (lit.,[5] 170–172 °C); ν_{max}/cm^{-1} 3452 and 1718; δ 0.90 (3 H, s, 18-H$_3$), 0.93 (3 H, s, 19-H$_3$), 2.06 (3 H, s, OAc), 4.02 (1 H, d, *J* 6.5, 6-H) and 5.25 (1 H, m, 3-H).

Reaction of 3β-*Acetoxy*-5α,6α-*epoxy*-7-*norandrostan*-17-*one* **9** *with Periodic Acid.*—A solution of the epoxide (300 mg) in acetone (9 cm^3) was treated with aq. periodic acid (70 mg, 7 cm^3) under reflux for 90 min. The solution was cooled, poured into water and the product was recovered in ethyl acetate. The extract was washed successively with aq. sodium hydrogen carbonate and water, and dried. The solvent was evaporated off to give a residue which was chromatographed on silica. Elution with 35% ethyl acetate–light petroleum gave 3β-acetoxy-5β,6α-dihydroxy-7-norandrostan-17-one **15** (260 mg), identical (IR and NMR) with the product obtained previously. Hydrolysis of the acetate in methanol with aq. sodium hydroxide at room temperature for 1 h gave 3β,5β,6α-trihydroxy-7-norandrostan-17-one **16**, identical (IR and NMR) with the material described above.

Reaction of 3β-*Acetoxy*-5α,6α-*epoxy*-7-*norandrostan*-17-*one* **9** *with Hydrogen Bromide in Glacial Acetic Acid.*—The epoxide (500 mg) was treated with 48% hydrogen bromide in glacial acetic acid (5 cm^3) at room temperature for 2 h. The mixture was poured into aq. sodium hydrogen carbonate and was then recovered in ethyl acetate. The extract was washed with water and dried. The solvent was evaporated off and the residue was chromatographed on silica. Elution with 2% ethyl acetate–light petroleum gave 3β,6-*dibromo*-6-*norandrost*-5-*en*-17-*one* **17** (100 mg), which was crystallized from ethyl acetate–light petroleum as needles, m.p. 175–177 °C (Found: C, 52.3; H, 5.5. $C_{18}H_{24}BrO_2$ requires C, 51.9; H, 5.8%); ν_{max}/cm^{-1} 1733 and 1635; δ 0.93 (3 H, s, 18-H$_3$), 0.96 (3 H, s, 19-H$_3$), 3.13 (1 H, ddd, *J* 2, 4.7 and 14, 4-H) and 3.88 [1 H, t (*J* 8) of t, (*J* 4), 3-H]. Further elution with 2% ethyl acetate–light petroleum gave 3β-*acetoxy*-6-*bromo*-7-*norandrost*-5-*en*-17-*one* **18** (150 mg), which was crystallized from ethyl acetate–light petroleum as needles, m.p. 140–142 °C (Found: C, 58.2; H, 7.0. $C_{20}H_{27}BrO_3 \cdot H_2O$ requires C, 58.1; H, 7.1%); ν_{max}/cm^{-1} 1747 and 1650; δ 0.93 (3 H, s, 18-H$_3$), 0.95 (3 H, s, 19-H$_3$), 2.04 (3 H, s, OAc) and 4.65 [1 H, t, (*J* 11.5) of t (*J* 4.5), 3-H]. Elution with 5% ethyl acetate–light petroleum gave 5β-*bromo*-3α,6α-*epoxy*-7-*norandrostan*-17-*one* **19** (200 mg), which was crystallized from ethyl acetate–light petroleum as needles, m.p. 120–121 °C (Found: C, 60.6; H, 6.7. $C_{18}H_{25}BrO_2$ requires C, 61.2; H, 7.1%); ν_{max}/cm^{-1} 1740; δ 0.93 (3 H, s, 18-H$_3$), 1.1 (3 H, s, 19-H$_3$), 4.19 (1 H, d, *J* 2, 6-H) and 4.52 (1 H, t, *J* 5.3, 3-H).

Reaction of 5β-*Bromo*-3α,6α-*epoxy*-7-*norandrostan*-17-*one* **19** *with Hydrogen Bromide in Glacial Acetic Acid.*—The steroid **19** (25 mg) was heated with 48% hydrogen bromide in glacial acetic acid (5 cm^3) under reflux for 15 min. The

Table 2 Fractional atomic co-ordinates ($\times 10^4$) with estimated standard deviations in parentheses for compound **17**

	x	*y*	*z*
Br(1)	1852.7(9)	−355.2(7)	1174.0(5)
Br(2)	6466.3(10)	−1020.0(8)	−1415.0(5)
O	2975(8)	−3121(5)	4750(3)
C(1)	7429(10)	−2168(7)	948(5)
C(2)	7721(9)	−1727(7)	93(5)
C(3)	6155(9)	−1523(6)	−311(4)
C(4)	5159(9)	−638(6)	123(4)
C(5)	5045(8)	−927(7)	992(4)
C(6)	3826(8)	−883(5)	1487(4)
C(8)	4247(9)	−1157(6)	2330(4)
C(9)	5714(8)	−1862(6)	2194(4)
C(10)	6497(8)	−1326(5)	1448(5)
C(11)	6624(9)	−2086(7)	2956(5)
C(12)	5555(9)	−2631(6)	3592(5)
C(13)	4072(9)	−1959(5)	3693(4)
C(14)	3197(9)	−1772(6)	2898(4)
C(15)	1565(10)	−1385(7)	3132(5)
C(16)	1229(10)	−2108(7)	3866(6)
C(17)	2804(11)	−2483(6)	4189(5)
C(18)	4427(11)	−844(7)	4140(5)
C(19)	7495(9)	−307(7)	1670(5)

Table 3 Intramolecular distances (Å) and angles (°) with estimated standard deviations in parentheses for compound **17**

(a) Bonds			
Br(1)–C(6)	1.885(7)	Br(2)–C(3)	1.961(7)
O–C(17)	1.219(9)	C(1)–C(2)	1.546(11)
C(1)–C(10)	1.535(10)	C(2)–C(3)	1.526(11)
C(3)–C(4)	1.543(10)	C(4)–C(5)	1.500(10)
C(5)–C(6)	1.337(10)	C(5)–C(10)	1.538(10)
C(6)–C(8)	1.494(10)	C(8)–C(9)	1.534(10)
C(8)–C(14)	1.503(10)	C(9)–C(10)	1.558(10)
C(9)–C(11)	1.519(10)	C(10)–C(19)	1.536(10)
C(11)–C(12)	1.550(11)	C(12)–C(13)	1.517(11)
C(13)–C(14)	1.544(10)	C(13)–C(17)	1.507(11)
C(13)–C(18)	1.559(11)	C(14)–C(15)	1.528(11)
C(15)–C(16)	1.531(12)	C(16)–C(17)	1.525(13)
(b) Angles			
C(2)–C(1)–C(10)	111.4(6)	C(1)–C(2)–C(3)	108.8(6)
Br(2)–C(3)–C(2)	110.3(5)	Br(2)–C(3)–C(4)	108.0(5)
C(2)–C(3)–C(4)	113.0(6)	C(3)–C(4)–C(5)	109.6(6)
C(4)–C(5)–C(6)	130.1(7)	C(4)–C(5)–C(10)	120.0(6)
C(6)–C(5)–C(10)	110.0(6)	Br(1)–C(6)–C(5)	123.1(6)
Br(1)–C(6)–C(8)	123.7(5)	C(5)–C(6)–C(8)	112.8(6)
C(6)–C(8)–C(9)	100.3(6)	C(6)–C(8)–C(14)	124.1(6)
C(9)–C(8)–C(14)	108.6(6)	C(8)–C(9)–C(10)	104.4(5)
C(8)–C(9)–C(11)	113.3(6)	C(10)–C(9)–C(11)	121.6(6)
C(1)–C(10)–C(5)	110.9(6)	C(1)–C(10)–C(9)	113.2(5)
C(1)–C(10)–C(19)	111.1(6)	C(5)–C(10)–C(9)	100.1(5)
C(5)–C(10)–C(19)	109.1(5)	C(9)–C(10)–C(19)	111.9(6)
C(9)–C(11)–C(12)	110.2(6)	C(11)–C(12)–C(13)	110.6(6)
C(12)–C(13)–C(14)	113.0(6)	C(12)–C(13)–C(17)	116.7(6)
C(12)–C(13)–C(18)	110.0(6)	C(14)–C(13)–C(17)	100.5(6)
C(14)–C(13)–C(18)	112.7(6)	C(17)–C(13)–C(18)	103.4(6)
C(8)–C(14)–C(13)	108.8(6)	C(8)–C(14)–C(15)	124.4(6)
C(13)–C(14)–C(15)	105.7(6)	C(14)–C(15)–C(16)	101.9(6)
C(15)–C(16)–C(17)	106.4(7)	O–C(17)–C(13)	126.7(8)
O–C(17)–C(16)	124.4(8)	C(13)–C(17)–C(16)	109.0(6)

Table 4 Fractional atomic co-ordinates ($\times 10^4$) with estimated standard deviations in parentheses for compound **14**

	x	*y*	*z*
Br(1)	1253(5)	4664(2)	3335(2)
Br(2)	2602(5)	8283(2)	2360(2)
O	9368(37)	3754(13)	5793(12)
C(1)	5982(45)	7536(15)	3695(14)
C(2)	6366(43)	7564(15)	2810(13)
C(3)	4652(44)	7343(16)	2338(15)
C(4)	3700(42)	6446(14)	2517(14)
C(5)	3394(35)	6311(13)	3377(12)
C(6)	3679(38)	5394(14)	3570(12)
C(8)	4290(36)	5330(15)	4407(13)
C(9)	5523(34)	6154(13)	4465(12)
C(10)	5051(38)	6652(13)	3906(11)
C(11)	6937(40)	6290(15)	5137(13)
C(12)	8190(42)	5482(16)	5337(13)
C(13)	6705(38)	4710(16)	5416(13)
C(14)	5659(36)	4581(15)	4608(12)
C(15)	4637(49)	3660(17)	4707(15)
C(16)	6493(56)	3206(19)	5121(17)
C(17)	7645(55)	3828(19)	5498(16)
C(18)	5334(48)	4829(17)	6088(15)
C(19)	1295(44)	6662(16)	3686(13)

Table 5 Intramolecular distances (Å) and angles (°) with estimated standard deviations in parentheses for compound **14**

(a) Bonds			
Br(1)–C(6)	2.01(2)	Br(2)–C(3)	2.01(3)
O–C(17)	1.25(4)	C(1)–C(2)	1.55(3)
C1()–C(10)	1.57(3)	C(2)–C(3)	1.43(4)
C(3)–C(4)	1.58(3)	C(4)–C(5)	1.51(3)
C(5)–C(6)	1.50(3)	C(5)–C(10)	1.52(3)
C(5)–C(19)	1.58(4)	C(6)–C(8)	1.50(3)
C(8)–C(9)	1.54(3)	C(8)–C(14)	1.53(3)
C(9)–C(10)	1.28(3)	C(9)–C(11)	1.50(3)
C(11)–C(12)	1.56(4)	C(12)–C(13)	1.57(4)
C(13)–C(14)	1.57(3)	C(13)–C(17)	1.53(4)
C(13)–C(18)	1.48(4)	C(14)–C(15)	1.61(4)
C(15)–C(16)	1.59(5)	C(16)–C(17)	1.40(5)
(b) Angles			
C(2)–C(1)–C(10)	109(2)	C(1)–C(2)–C(3)	115(2)
Br(2)–C(3)–C(2)	110(2)	Br(2)–C(3)–C(4)	113(2)
C(2)–C(3)–C(4)	115(2)	C(3)–C(4)–C(5)	112(2)
C(4)–C(5)–C(6)	110(2)	C(4)–C(5)–C(10)	116(2)
C(4)–C(5)–C(19)	113(2)	C(6)–C(5)–C(10)	97(2)
C(6)–C(5)–C(19)	112(2)	C(10)–C(5)–C(19)	108(2)
Br(1)–C(6)–C(5)	114(2)	Br(1)–C(6)–C(8)	112(2)
C(5)–C(6)–C(8)	108(2)	C(6)–C(8)–C(9)	99(2)
C(6)–C(8)–C(14)	115(2)	C(9)–C(8)–C(14)	109(2)
C(8)–C(9)–C(10)	110(2)	C(8)–C(9)–C(11)	120(2)
C(10)–C(9)–C(11)	130(2)	C(1)–C(10)–C(5)	117(2)
C(1)–C(10)–C(9)	129(2)	C(5)–C(10)–C(9)	114(2)
C(9)–C(11)–C(12)	113(2)	C(11)–C(12)–C(13)	109(2)
C(12)–C(13)–C(14)	107(2)	C(12)–C(13)–C(17)	118(2)
C(12)–C(13)–C(18)	110(2)	C(14)–C(13)–C(17)	98(2)
C(14)–C(13)–C(18)	116(2)	C(17)–C(13)–C(18)	107(2)
C(8)–C(14)–C(13)	111(2)	C(8)–C(14)–C(15)	118(2)
C(13)–C(14)–C(15)	102(2)	C(14)–C(15)–C(16)	98(2)
C(15)–C(16)–C(17)	108(3)	O–C(17)–C(13)	119(3)
O–C(17)–C(16)	128(3)	C(13)–C(17)–C(16)	112(3)

solution was poured into aq. sodium hydrogen carbonate and the steroids were recovered in ethyl acetate. The extract was dried and the solvent was evaporated off to afford a residue, which was chromatographed on silica. Elution with 2% ethyl acetate–light petroleum gave 3β,6-dibromo-6-norandrost-5-en-17-one **17** (17 mg), which was identified by its IR and NMR spectrum.

3β-*Methylsulphonyloxy*-7-*norandrost*-5-*en*-17-*one* **6**.—A solution of 3β-hydroxy-7-norandrost-5-en-17-one **8** (700 mg) in dry pyridine (10 cm^3) was treated with methanesulphonyl chloride (2 cm^3) for 2 h. The mixture was poured into dil. hydrochloric acid and the products were recovered in ethyl acetate. The extract was washed successively with aq. sodium hydrogen carbonate and water, and was then dried. The solvent was evaporated off to afford 3β-*methylsulphonyloxy*-7-*norandrost*-5-*en*-17-*one* **6** (650 mg), which was crystallized from ethyl acetate–light petroleum as needles, m.p. 162–

Table 6 Fractional atomic co-ordinates ($\times 10^4$) with estimated standard deviations in parentheses for compound **20**

	x	*y*	*z*
O	1 253(5)	7 791	6 487(3)
C(1)	−7 069(7)	10 690(8)	9 085(3)
C(2)	−8 543(7)	11 870(9)	9 272(4)
C(3)	−8 919(7)	13 539(8)	8 787(4)
C(4)	−7 854(7)	14 073(8)	8 112(4)
C(5)	−6 386(6)	12 899(7)	7 918(3)
C(6)	−4 980(7)	13 232(7)	7 253(4)
C(8)	−4 273(7)	11 259(7)	7 114(3)
C(9)	−4 208(6)	10 386(7)	8 094(3)
C(10)	−6 010(7)	11 221(7)	8 405(3)
C(11)	−3 857(7)	8 303(7)	8 057(3)
C(12)	−1 938(7)	7 926(7)	7 672(4)
C(13)	−1 963(6)	8 866(7)	6 726(3)
C(14)	−2 315(7)	10 970(7)	6 810(3)
C(15)	−1 825(8)	11 782(9)	5 905(4)
C(16)	−9(8)	10 681(9)	5 771(4)
C(17)	−52(7)	8 939(9)	6 351(4)
C(18)	−3 439(7)	7 943(10)	5 917(4)
C(19)	−6 684(8)	8 922(9)	9 654(4)

Table 7 Intramolecular distances (Å) and angles (°) with estimated standard deviations in parentheses for compound **20**

(a) Bonds			
O–C(17)	1.220(6)	C(1)–C(2)	1.401(8)
C(1)–C(10)	1.379(7)	C(1)–C(19)	1.517(8)
C(2)–C(3)	1.398(8)	C(3)–C(4)	1.377(8)
C(4)–C(5)	1.399(7)	C(5)–C(6)	1.505(8)
C(5)–C(10)	1.405(7)	C(6)–C(8)	1.545(7)
C(8)–C(9)	1.525(7)	C(8)–C(14)	1.518(7)
C(9)–C(10)	1.531(7)	C(9)–C(11)	1.540(7)
C(11)–C(12)	1.561(7)	C(12)–C(13)	1.506(7)
C(13)–C(14)	1.562(7)	C(13)–C(17)	1.525(7)
C(13)–C(18)	1.536(7)	C(14)–C(15)	1.514(8)
C(15)–C(16)	1.537(8)	C(16)–C(17)	1.517(9)
(b) Angles			
C(2)–C(1)–C(10)	118.0(5)	C(2)–C(1)–C(19)	118.6(5)
C(10)–C(1)–C(19)	123.3(5)	C(1)–C(2)–C(3)	120.9(5)
C(2)–C(3)–C(4)	121.0(5)	C(3)–C(4)–C(5)	118.4(5)
C(4)–C(5)–C(6)	127.8(5)	C(4)–C(5)–C(10)	120.5(5)
C(6)–C(5)–C(10)	111.6(4)	C(5)–C(6)–C(8)	101.1(4)
C(6)–C(8)–C(9)	103.0(4)	C(6)–C(8)–C(14)	119.3(4)
C(9)–C(8)–C(14)	109.5(4)	C(8)–C(9)–C(10)	102.6(4)
C(8)–C(9)–C(11)	110.9(4)	C(10)–C(9)–C(11)	123.1(4)
C(1)–C(10)–C(5)	121.1(5)	C(1)–C(10)–C(9)	131.9(5)
C(5)–C(10)–C(9)	106.7(4)	C(9)–C(11)–C(12)	109.7(4)
C(11)–C(12)–C(13)	111.8(4)	C(12)–C(13)–C(14)	110.7(4)
C(12)–C(13)–C(17)	118.0(4)	C(12)–C(13)–C(18)	111.0(4)
C(14)–C(13)–C(17)	98.8(4)	C(14)–C(13)–C(18)	113.4(4)
C(17)–C(13)–C(18)	104.6(4)	C(8)–C(14)–C(13)	108.7(4)
C(8)–C(14)–C(15)	123.4(4)	C(13)–C(14)–C(15)	104.7(4)
C(14)–C(15)–C(16)	103.2(5)	C(15)–C(16)–C(17)	105.4(5)
O–C(17)–C(13)	126.2(5)	O–C(17)–C(16)	124.6(5)
C(13)–C(17)–C(16)	109.3(4)		

164 °C (Found: C, 64.95; H, 7.7. $C_{19}H_{28}O_4S$ requires C, 64.7; H, 8.0%); ν_{max}/cm^{-1} 1730; δ(90 MHz) 0.9 (6 H, s, 18- and 19-H_3), 3.0 (3 H, s, OMs), 4.5 (1 H, m, 3-H) and 5.6 (1 H, s, 6-H).

3β-Methylsulphonyloxy-5α,6α-epoxy-7-norandrostan-17-one **10**.—A solution of MCPBA (400 mg) in chloroform (5 cm^3) was added dropwise during 30 min to a solution of 3β-methylsulphonyloxy-7-norandrost-5-en-17-one **6** (700 mg) in chloroform (20 cm^3) at room temperature. The mixture was left overnight and then aq. sodium sulphite was added to the vigorously stirred mixture until a negative starch–iodide test was obtained. The solution was diluted with chloroform, washed successively with aq. sodium hydrogen carbonate and water, and dried. The solvent was evaporated off to afford 3β-*methylsulphonyloxy-5α,6α-epoxy-7-norandrostan-17-one* **10** (680 mg), which was crystallized from ethyl acetate–light petroleum as needles, m.p. 94–95 °C (Found: C, 62.1; H, 7.4. $C_{19}H_{24}O_5S$ requires C, 61.9; H, 7.6%); ν_{max}/cm^{-1} 1734; δ 0.87 (3 H, s, 18-H_3), 0.94 (3 H, s, 19-H_3), 3.02 (3 H, s, OMs), 3.40 (1 H, br s, 6-H) and 4.87 [1 H, t (*J* 11.5) of t (*J* 5.2), 3-H].

Reaction of 3β-Methylsulphonyloxy-5α,6α-epoxy-7-norandrostan-17-one **10** *with Hydrogen Bromide in Glacial Acetic Acid*.—The epoxide **10** (2 g) was heated with 48% hydrogen bromide in glacial acetic acid (20 cm^3) under reflux for 15 min. The mixture was poured into aq. sodium hydrogen carbonate and the products were recovered in ethyl acetate. The extract was washed successively with aq. sodium hydrogen carbonate and water, and was then dried. The solvent was evaporated off to give a residue, which was chromatographed on silica. Elution with 5% ethyl acetate–light petroleum gave 3β,6β-*dibromo-5β-methyl-7,19-dinorandrost-9-en-17-one* **14** (200 mg), which was crystallized from light petroleum as needles, m.p. 140–142 °C (Found: C, 52.2; H, 5.7. $C_{18}H_{24}Br_2O$ requires C, 51.9; H, 5.8%); ν_{max}/cm^{-1} 1735; δ 0.94 (3 H, s, 18-H_3), 1.36 (3 H, s, 19-H_3), 3.63 (1 H, d, *J* 8.7, 6-H) and 4.63 (1 H, pentuplet, *J* 3.6, 3-H). Further elution, with 7% ethyl acetate–light petroleum, gave 3β,6-dibromo-7-norandrost-5-en-17-one **17** (200 mg), identical (IR, NMR) with the product obtained previously. Further elution, with 10% ethyl acetate–light petroleum, gave *1-methyl-7-norestra-1,3,5(10)-trien-17-one* **20** (500 mg), which was crystallized, with difficulty, from ethyl acetate–light petroleum as needles, m.p. 215–216 °C (Found: C, 80.0; H, 8.1. $C_{18}H_{22}O{\cdot}H_2O$ requires C, 79.5; H, 8.7%); ν_{max}/cm^{-1} 1736; δ 0.93 (3 H, s, 18-H_3), 2.37 (3 H, s, ArMe), 6.90 (1 H, d, *J* 7.5), 7.03 (1 H, t, *J* 7.5) and 7.08 (1 H, d, *J* 7.5) (each ArH).

Crystal-structure Determinations.—A summary of the crystal data and structure-refinement details are given in Table 1. In each case data were collected from a crystal mounted on an Enraf–Nonius CAD4 diffractometer operating in the θ–2θ mode with $\Delta\theta = (0.8 + 0.35 \tan\theta)°$ and a maximum scan time of one minute and with monochromated Mo-$K\alpha$ radiation (λ = 0.710 69 Å). Unique reflections were measured for $2 < \theta < 25°$ and those reflections with $|F^2| > \sigma(F^2)$ were used in the refinement where $\sigma(F^2) = \{\sigma^2(I) + (0.04I)^2\}^{\frac{1}{2}}/L_p$. Absorption corrections were applied using DIFABS[10] after isotropic refinement.

Structures were solved either by routine heavy-atom methods for the Br-containing compounds, or by direct methods using MULTAN.[11] Refinement was by full-matrix least-squares with non-hydrogen atoms anisotropic and weights of $w = 1/\sigma^2(F)$. Hydrogen atoms, where included, were given fixed isotropic thermal parameters of $U_{iso} = 1.3U_{eq}$ for the parent atom. Programs from the Enraf–Nonius SDP-Plus package were run on a microVax computer. Scattering factors were those implemented in the program package with anomalous dispersion components included at all times. Tables of fractional atomic co-ordinates and bond lengths and angles are given in Tables 2 and 3 (compound **17**), 4 and 5 (compound **14**), and 6 and 7 (compound **20**).*

* *Supplementary data* (see section 5.6.3 of Instructions for Authors, issue 1). The remaining crystallographic tables for these compounds have been deposited with the Cambridge Crystallographic Data Centre.

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