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HIGHER ISOPRENOIDS—III

DEGRADATION OF ISO-OCTENYL SIDE-CHAIN OF TETRACYCLIC TRITERPENOIDS—A NOVEL APPROACH*

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Abstract—A novel efficient sequence of reactions, by which 9,19-cyclo-4,4,14α-trimethyl-3β-acetoxy-5α,9β-pregnan-20-one (V) and 9,19-cyclo-4,4,14α-trimethyl-3β-acetoxy-5α,9β-androstan-17-one (VI) can be obtained from cycloartenol (I) in overall yields of over 42% and 38% respectively, is reported.

THE conversion of tetracyclic triterpenoids into steroidal hormone analogues has been a subject of considerable activity[1] and still continues to attract attention.[2] Cycloartenol (I), though widely distributed in nature,[3] has till now been difficult to obtain, but we now find that it can be readily obtained from Indian opium marc (Experimental). In view of this, it was thought of interest to convert it into steroid hormone analogues, such as III and IV; it may be further noted that these compounds or their earlier intermediates should be amenable[4] to C_9/C_{11} substitution with concomitant cyclopropane ring fission to a C_{19}—Me. As a first step, we have investigated the systematic degradation of its side-chain, and we now report on a novel and efficient sequence of reactions, by which 9,19-cyclo-4,4,14α-trimethyl-3β-acetoxy-5α,9β-pregnan-20-one (V) and 9,19-cyclo-4,4,14α-trimethyl-3β-acetoxy-5α,9β-androstan-17-one (VI) can be obtained from I in overall yields of 42% and 38% respectively.

Side-chain degradation of cycloartenol

By following a recently described procedure (ozonolysis–CrO_3 oxidation),[5] cycloartenyl acetate (II) could be degraded to the known[6] tris-nor acid VII, in ~80% yield. Further degradation of the side chain was first attempted by the Meystre–Miescher modification[7] of the Barbier–Wieland method. Action of excess phenyl magnesium bromide on the hydroxy ester (VIII), followed by refluxing of the product with AcOH–Ac_2O gave the required diphenyl ethylene (X) in 77% yield, besides another compound (yield 20%). This latter compound analyses for $C_{37}H_{54}O_4$ (M^+, $m/e = 562$) and in view of its spectral characteristics [IR(CCl_4): C=O 1740 cm^{-1}; OAc 1240, 1250 cm^{-1}. PMR:† two OAc (6H, singlets at 1·98 and 2·0 ppm); —CHOAc (1H multiplet centred at 4·51 ppm); $\oint$—CHOAc (1H multiplet centred at 5·63 ppm); C_6H_5 (5H singlet at 7·36 ppm)] is assigned structure XI‡ this formulation is supported by Jones oxidation[9] of the derived diol to a phenyl ketone (λ_{max} 238 mμ, ε 11400; cf. e.g. $PhCO.CH_2CH_3$ [10] λ_{max} 238 mμ, ε 11450) which should be XII.

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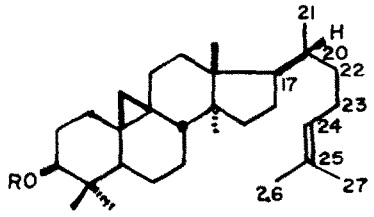
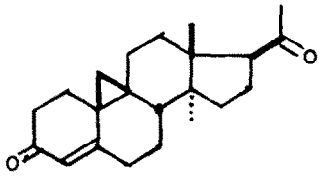
† Chemical shifts are expressed as ppm in δ values.

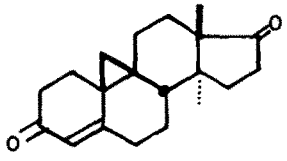
‡ This compound obviously arises from the intermediate phenyl ketone by reduction. Evidently reduction in the present case has occurred due to magnesions bromide.[8]



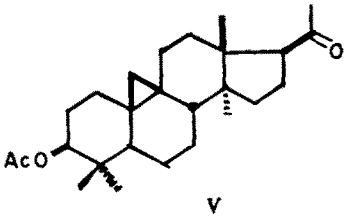
I: R = H
II: R = Ac



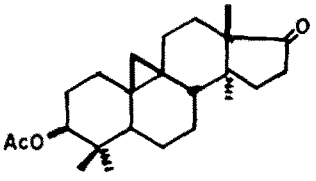
III



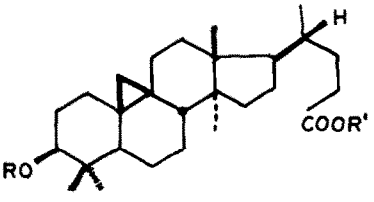
IV



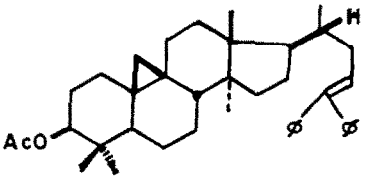
V



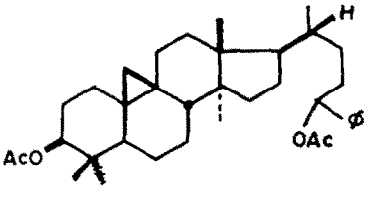
VI



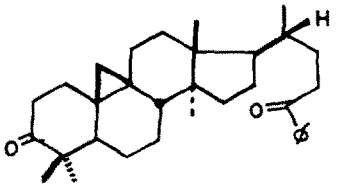
VII: R = AC, Ŕ = H
VIII: R = H, Ŕ = Me
IX: R = R′ = H



X



XI

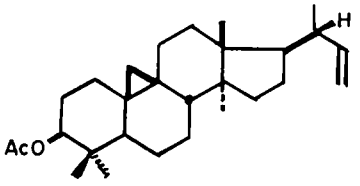


XII

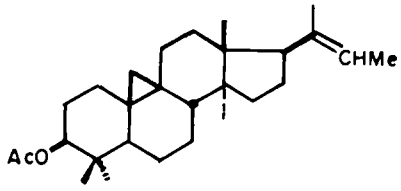
In spite of several efforts, allylic bromination (NBS,[11] 1,3-dibromo-5,5-dimethylhydantoin)[12] of olefin X, followed by dehydrobromination (1,5-diazabicyclo[5.4.0]undec-5-ene)[13] furnished only poor yields of impure dehydro derivative (λ_{max} 305 mμ, ε 14,000–18,000; expected[14] ε ~30,000) which could not be easily purified and hence this route had to be abandoned.

The route next investigated proved most successful.

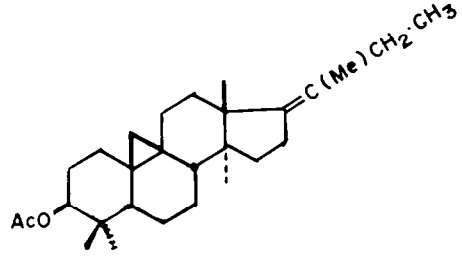
The tris-nor acid (VII), on Cu^{++}-catalysed[15] oxidative decarboxylation with $Pb(OAc)_4$ in refluxing benzene containing some pyridine, smoothly furnished in over 95% yield the expected olefin XIII (M^+, $m/e = 412$; IR: —CH=CH_2 1650, 990, 912 cm^{-1}; —$OCOCH_3$ 1738, 1255 cm^{-1}; PMR: cyclopropane methylene, a pair of doublets centred at 0·32 and 0·6 ppm, $J = 4$ Hz; —C<u>H</u>=C<u>H</u>$_2$, characteristic ABC-type 3H multiplet located between 4·68–5·76 ppm). On exposure to N-lithioethylenediamine,[16] this olefin (XIII) could be isomerized essentially either to XIV or XV. Thus, 12 min reaction at 120–125° (bath temp) gave a product, which after acetylation (Ac_2O–pyridine) furnished in 95% yield XIV (IR: —C=CH— 840 cm^{-1}; —$OCOCH_3$ 1740, 1260 cm^{-1}; PMR: cyclopropane methylene, a pair of doublets centred at 0·3 and 0·6 ppm, $J = 4$ Hz; C<u>H</u>$_3$—C=CH—C<u>H</u>$_3$, overlapping, a broad singlet at 1·56 ppm and an unresolved doublet centred at 1·66 ppm; —C=C<u>H</u>—CH_3, 1H multiplet centred at 5·18 ppm). On



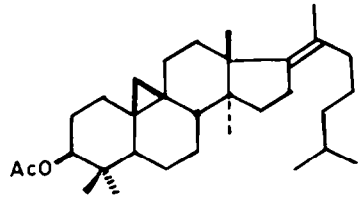
XIII



XIV



XV



XVI

the other hand, when the reaction period was extended to 15 hr, the crude product acetylated and then worked up, olefin XV (PMR: cyclopropane methylene, a pair of doublets centred at 0·3 and 0·62 ppm, $J = 4$ Hz; —C=C(C<u>H</u>$_3$)C<u>H</u>$_2$CH$_3$, overlapping 5H signals between 1·53–1·73 ppm; no olefinic absorption) could be obtained in over 90% yield.

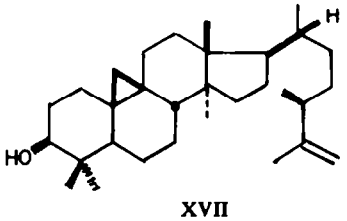
Ozonolysis of XIV, followed by oxidative work-up[5] with Jones reagent, furnished in ~60% yield a product, characterized as the desired hexanor-ketone V (M^+, $m/e = 400$; IR: C=O 1730, 1700 cm^{-1}; PMR: cyclopropane methylene, a pair of doublets centred at 0·32 and 0·62 ppm, $J = 4$ Hz; two C<u>H</u>$_3$.CO, two 3H singlets at 1·98 and 2·01 ppm; four quaternary Me's, 9H singlet at 0·85 ppm and a 3H singlet at 0·9 ppm; —<u>H</u>C—C=O,[17] 1H deformed triplet centred at 2·9 ppm, $J = 8$ Hz).

The tetrasubstituted olefin XV, proved rather resistant to ozonolysis, as ozonolysis–Jones oxidative work-up gave the required andrastanone (VI) in only 25% yield. This conversion was best effected by hydroxylation (OsO_4/H_2S), followed by $Pb(OAc)_4$ cleavage, when the octanor-ketone VI (M^+, m/e = 372. IR: C=O 1740 cm^{-1}: PMR · cyclopropane methylene, a pair of doublets centred at 0·32 and 0·66 ppm, J = 4 Hz; four quaternary Me's, 9H singlet at 0·85 ppm and a 3H singlet at 1·1 ppm; O=C—C<u>H</u>$_2$, 2H, broad triplet centred at 2·16 ppm, J = 6 Hz) was obtained in ~70% yield.

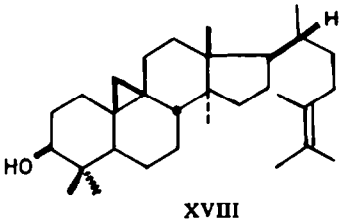
The success with the isomerization–oxidation sequence, prompted us to apply this sequence directly to cycloartenyl acetate (II), with satisfactory results. Thus, exposure of II to N-lithio-ethylene-diamine at 120–125° for 15 hr gave a product consisting essentially (after acetylation) of three components ($AgNO_3$–silica gel TLC).[18] This material, without separation, was subjected to hydroxylation (OsO_4/H_2S) and the product separated into an unreactive olefin (~40%) and a mixture of diols. $Pb(OAc)_4$ cleavage of diol mixture furnished the required hexanor-ketone V (12%) and the octanor-ketone VI (6%). The unreacted olefin was suspected to be 3β-acetoxy-cycloart-17 (20)-ene (XVI) and this was indeed borne out from its spectral characteristics (M^+, m/e = 468. PMR: cyclopropane methylene, a pair of doublets centred at 0·3 and 0·61 ppm, J = 4 Hz; four quaternary Me's at 0·81, 0·81, 0·81 and 1·1 ppm; (<u>Me</u>)$_2$CH—, doublet centred at 0·86 ppm, J = 7 Hz; —C=C(C<u>H</u>$_3$)C<u>H</u>$_2$—, overlapping signals between 1·56–1·66 ppm; no olefinic absorption).

*Side-chain degradation of cyclolaudenol**

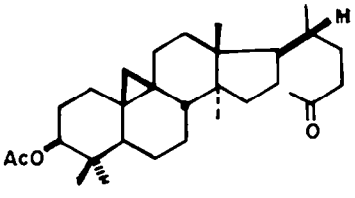
The above sequence of reaction has been suitably modified and applied to cyclolaudenol (XVII) another readily accessible triterpene from *Opium marc.*[19] Cyclolaudenol on exposure to N-lithio-ethylenediamine at 120–125° gave the isopropylidene isomer (XVIII) in 92% yield. Structure XVIII is fully supported by its PMR spectrum: cyclopropane methylene, pair of doublets centred at 0·32 and 0·58 ppm, J = 4 Hz; quaternary Me's at 0·78, 0·91, 0·95, 0·95 ppm; three vinylic Me's, 9H singlets at 1·8 ppm; no olefinic proton.



XVII



XVIII



XIX

* This work, in part, was carried out by Dr. K. D. Pathak.

Ozonolysis of the acetate derived from XVIII gave in 85% yield the known[20] methyl ketone (XIX); this ketone had been prepared earlier[20] by a 5-step sequence from cyclolaudenol. NaOBr oxidation of XIX yielded the trisnor-acid IX, already obtained earlier from cycloartenol, and degraded to either V or VI. Incidentally, degradation of cyclolaudenol to the trisnor-acid provides a new direct correlation of cyclolaudenol with cycloartenol, an objective which had been realized earlier by a different sequence.[20]

EXPERIMENTAL

All m.ps are uncorrected. Light petroleum refers to the fraction b.p. 40–60°. Optical rotations were measured in $CHCl_3$.

UV spectra were taken on a Perkin–Elmer spectrophotometer, model 350, in hexane. IR spectra were recorded as Nujol mulls on a Perkin–Elmer Infracord model 137E. PMR spectra were taken in CCl_4, on a Varian A-60 spectrometer, using TMS as the internal standard; chemical shifts are expressed in ppm (δ) relative to TMS as zero. Mass spectra were recorded on a CEC mass spectrometer, model 21-110B, using an ionizing potential of 70 eV and a direct inlet system; besides, the molecular ion, ten most abundant ions are mentioned with their relative intensities.

Silica gel for column chromatography was of 100–200 mesh and was activated at 130–140° (6 hr) and then standardized[21] $AgNO_3$-impregnated silica gel was made by the method of Gupta and Dev[18] and activated at 100–110° (4 hr). TLC was carried out on silica gel or silica gel–$AgNO_3$ (10% $AgNO_3$) layers (0·3 mm) containing 15% gypsum; the plates were activated at 100–110° (45 min) and then stored in a desiccator. Conc. H_2SO_4 spray, followed by heating (120°, 5 min) was used for visualization of TLC spots.

Isolation of cycloartenol and cyclolaudenol from Opium marc

*Opium marc** light petroleum extract (2·6 kg) was dissolved in C_6H_6 (6·3 l.) and with stirring diluted with EtOH (1·4 l.). After 2 hr. the dark soln was decanted off from tar and freed of solvent to give a material (1·6 kg) which was refluxed (12 hr) with 10% ethanolic KOH (4 l.). The saponified material was freed of solvent to give a waxy cake (2 kg). This material (0·5 kg) was suspended in water (2·5 l), extracted with EtOAc (500 ml × 2) and the EtOAc extract worked up to afford a neutral gum (150 g). TLC (solvent: 5% EtOAc in C_6H_6) showed four spots with R_f 0·88, 0·53, 0·36 (major) and 0·23. The gum was refluxed with acetone (1 l.) containing 10% light petroleum, charcoaled, concentrated to ~600 ml and the solids (30 g, m.p. 118–120°) collected after 12 hr at 4°; two concentrations of the mother liquors furnished two additional crops (10 g, m.p. 116–120°; 5 g, m.p. 114–120°). The mother liquor was treated for the isolation of cycloartenol, as described below. The combined solids were charcoaled in ether, the clarified filtrate concentrated and diluted with MeOH, when cyclolaudenol (27 g, m.p. 120–121°) slowly crystallized out; recrystallization from acetone gave pure cyclolaudenol (17 g), m.p. 124–126°, $[\alpha]_D$ +46° (*c* 2·0%). (Lit.[20]: m.p. 125°, $[\alpha]_D$ +46°).

The crude cyclolaudenol mother liquor was charcoaled, the clarified filtrate concentrated to ~200 ml, and diluted with MeOH. After several hours at 4°, the separated crystalline solids (47 g, m.p. 80–90°) were collected. Repeated crystallizations of this material from ether–MeOH gave pure cycloartenol (13 g), m.p. 112–114° (after thorough drying), $[\alpha]_D$ +52° (*c* 2%); PMR: cyclopropane methylene (a pair of doublets centred at 0·3 and 0·56 ppm, $J = 4$ Hz); quaternary Me's at 0·75, 0·88, 0·91 and 0·93 ppm; two vinylic Me's (broad singlets at 1·58 and 1·65 ppm; —C<u>H</u>OH (1H broad triplet centred at 3·16 ppm, $J = 5$ Hz); —C=C<u>H</u>— (1H triplet centred at 5·1 ppm, $J = 7$ Hz). (Lit.: m.p. 85–92°,[4a] 99° (solv.), 115° (anhy.);[6] $[\alpha]_D$ +48° and 54° respectively).

Acetate (Ac_2O–pyridine) m.p. 120–121°, $[\alpha]_D$ +57° (*c* 5·2%) (Lit:[4a] m.p. 122·5–123·5°, $[\alpha]_D$ +58°).

3β-*Acetoxy*-9, 19-*cyclo*-25,26,27-*trisnor*-*lanost*-24-*oic acid* (VII)

Cycloartenyl acetate (5·0 g) in $CHCl_3$ (250 ml) was ozonized at −10° and the crude "ozonide" isolated by solvent removal at room temp, under vacuum. This was taken up in acetone (10 ml., cooled (0°) and Jones reagent[9] (prepared by dissolving 2·6 g of chromic trioxide in 2·3 ml conc H_2SO_4, diluted with H_2O to a volume of 10 ml) introduced dropwise with cooling and stirring till a brown colour persisted (5 ml). After 5 min at room temp, the reaction mixture was diluted with water (100 ml), extracted with ether (80 ml × 3) and separated with NaOH aq (5%) into acidic (3·8 g, m.p. 206–210°) and neutral (~10%) fractions. The

* Supplied by Opium Alkaloid Works, Ghazipur.

acidic fraction was recrystallized from CH_3OH–ether to give pure VII, m.p. 215–217°, $[\alpha]_D$ +44·6° (*c* 1·2%). (Found: C, 75·67; H, 10·32. $C_{29}H_{46}O_4$ requires: C, 75·94; H, 10·11%). (Lit:[6] m.p. 221·5–223°, $[\alpha]_D$ +62°).

Hydrolysis (10% ethanolic NaOH, 4 hr reflux) of the above acetate furnished, after usual work-up, the crude hydroxy acid (IX) which was esterified (CH_2N_2, ether) and the product recrystallized from MeOH–ether to give pure *hydroxy ester* (VIII), m.p. 129–131°, $[\alpha]_D$ +67° (*c*, 1.9%). (Found: C, 78·48; H, 10·92. $C_{28}H_{46}O_3$ requires: C, 78·1; H, 10·77%).

3β-*Acetoxy*-9,19-*cyclo*-24,24-*diphenyl*-25,26,27-*trisnor*-*lanost*-23-*ene* (X)

The above hydroxy ester VIII (4·3 g) in dry benzene (150 ml) was added dropwise (1 hr) to a stirred (N_2) ether soln of PhMgBr (from Mg 3·6 g, C_6H_5Br 23·6 g; ether 100 ml) and the reaction mixture stirred and gently refluxed for 20 hr, after which it was worked up in the usual manner with NH_4Claq (400 ml). The product after solvent removal was steam-distilled to remove diphenyl and the non-volatile material taken up in ether. Solvent removal gave a gum (5·8 g), which was dehydrated by heating (4 hr) with AcOH (40 ml)–Ac_2O (8 ml). Excess AcOH–Ac_2O was flashed off under *vacuo* and the residue worked up with water in the usual manner to yield a product (6·1 g), which was chromatographed on SiO_2–gel/IIa (49 cm × 3·5 cm): (i) 2% C_6H_6 in light petroleum (500 ml × 3), 0·15 g, rejected; (ii) 15% C_6H_6 in light petroleum (500 ml × 5), 4·5 g, m.p. 130–140°; (iii) 50% C_6H_6 in light petroleum (200 ml), 0·12 g; (iv) C_6H_6 (200 ml × 5), 1·2 g, m.p. 122–124°.

Fraction (ii) was crystallized from MeOH–ether to give pure X, m.p. 148–151°, $[\alpha]_D$ +60·6° (*c*, 0·6%); IR: ϕ–R 1600, 1500, 763, 700 cm^{-1}; —$OCOCH_3$ 1740, 1240 cm^{-1}; PMR: —$OCOC\underline{H}_3$ (3H, s at 1·95 ppm; —$C\underline{H}$—OAc (1H, m centred at 4.46 ppm); —CH_2—$C\underline{H}$=$C(\phi)_2$ (1H, tr centred at 6·03 ppm, J = 9 Hz); two $C_6\underline{H}_5$ (10H, broad s at 7·11 ppm). Mass: *m/e* 578 (M^+: 8%), 193 (100%), 43 (48%), 91 (43%), 115 (36%), 55 (33%), 95 (29%), 69 (26%), 167 (25%), 180 (23%), 107 (20%). (Found: C, 84·74; H, 9·47. $C_{41}H_{54}O_2$ requires: C, 85·07; H, 9·4%).

Fraction (iv) was crystallized from MeOH–ether to give pure XI, m.p. 126–128°, $[\alpha]_D$ + 68·5° (*c*, 0·9%). Mass: *m/e* 562 (M^+; 3%), 91 (100%), 43 (92%), 95 (73%), 105 (62%), 117 (62%), 121 (49%), 69 (46%), 81 (46%), 145 (46%), 502 (43%). (Found: C, 78·66; H, 9·56. $C_{37}H_{54}O_4$ requires: C, 78·96; H, 9·67%).

9,19-*Cyclo*-24-*phenyl*-25,26,27-*trisnor*-*lanost*-3,24-*dione* (XII)

Hydrolysis (10% EtOH–KOH, 3 hr, reflux) of XI (0·6 g) furnished, after usual work-up, a diol (0·48 g), which on oxidation with Jones reagent afforded a compound (0·4 g, m.p. 148–154°). Crystallization from MeOH–ether furnished pure XII, m.p. 153–154°, $[\alpha]_D$ +45° (*c*, 1·3%); IR: C=O 1710, 1690 cm^{-1}; ϕ–R 1600, 1455, 765, 690 cm^{-1}; PMR: cyclopropane methylene (a pair of d centred at 0·18 and 0·53 ppm, J = 5 Hz); quaternary Me's at 0·91, 1·0, 1·01 and 1·05 ppm; $C_6\underline{H}_5$ (3H, m located between 7·36–7·56 ppm and a 2H, m located between 7·68–8·0 ppm. (Found: C, 83·2; H, 9·75. $C_{33}H_{46}O_2$ requires: C, 83·49; H, 9·77%).

3β-*Acetoxy*-9,19-*cyclo*-24,25,26,27-*tetranor*-*lanost*-22-*ene* (XIII)

A mixture of VII (1·5 g), $Pb(OAc)_4$ (2·56 g), $Cu(OAc)_2$ (0·132 g), pyridine (0·105 g) in dry benzene (150 ml) was stirred under reflux (4 hr, N_2). Excess of $Pb(OAc)_4$ was destroyed by addition of ethylene glycol (5 ml) and the reaction mixture worked up with ether (70 ml × 3) and separated with 5% NaOH aq into acidic (VII, 0·56 g, m.p. 212–215°) and neutral portions (0·82 g, m.p. 162–164°). Neurtal portion was crystallized from MeOH—ether to furnish pure XIII, m.p. 170–171°, $[\alpha]_D$ +46·1° (*c*, 1·3%). (Found: C, 81·41; H, 10·85. $C_{28}H_{44}O_2$ requires: C, 81·5; H, 10·75%).

3β-*Acetoxy*-9,19-*cyclo*-24,25,26,27-*tetranor*-*lanost*-20(22)-*ene* (XIV)

The olefin XIII (1·5 g) was added in one lot to a stirred soln of N-lithioethylenediamine complex[16a] (Li 2 g, $NH_2.CH_2.CH_2.NH_2$ 60 ml; N_2) at 120–125° (bath temp) and the reaction mixture maintained at this temp for 12 min. The product obtained after usual work-up[16a] was directly acetylated (pyridine–Ac_2O) to give the crude acetate as solid (1·49 g, m.p. 132–137°). This was recrystallized from MeOH–ether to afford pure XIV, m.p. 146–147°, $[\alpha]_D$ +50° (*c*, 1%). (Found: C, 81·47; H, 11·08. $C_{28}H_{44}O_2$ requires: C, 81·5; H, 10·75%).

3β-*Acetoxy*-9,19-*cyclo*-24,25,26,27-*tetranor*-*lanost*-17(20)-*ene* (XV)

The olefin XIII (1·5 g) was added in one lot to a stirred soln of N-lithioethylenediamine complex (Li 2 g, $NH_2.CH_2.CH_2.NH_2$ 60 ml; N_2) at 120–125° (bath temp) and the reaction mixture maintained at this temp

for 15 hr. The product obtained after usual work-up was directly acetylated (pyridine–Ac_2O) to give the crude acetate as solid (1·49 g, m.p. 118–124°). This was recrystallized from AcOH to furnish pure XV, m.p. 155–157°, $[\alpha]_D$ +34·5° (*c*, 1·6%). (Found: C, 81·74; H, 10·71. $C_{28}H_{44}O_2$ requires: C, 81·5; H, 10·75%).

9,19-*Cyclo*-4,4,14α-*trimethyl*-3β-*acetoxy*-5α,9β-*pregnan*-20-*one* (V)

The olefin XIV (0·618 g) in dry $CHCl_3$ (100 ml) was ozonized at −10°. The crude "ozonide" isolated by solvent removal at room temp. under *vacuo*, on oxidation with Jones reagent[5] furnished a neutral fraction (0·585 g), which was chromatographed on SiO_2–gel/I (13 cm × 2 cm): (i) 10% C_6H_6 in light petroleum (100 ml × 2), 0·053 g, rejected; (ii) benzene (100 ml × 5), 0·36 g, m.p. 150–151°; (iii) 5% MeOH in C_6H_6 (100 ml × 2), 0·15 g, rejected.

Fraction (ii) was crystallized from MeOH–ether to give pure V, m.p. 153–154°, $[\alpha]_D$ + 108° (*c*, 0·85%). Mass: *m/e* 400 (M^+; 4%), 271 (100%), 133 (74%), 122 (72%), 340 (70%), 123 (64%), 147 (63%), 135 (62%), 134 (62%), 297 (48%), 175 (48%). (Found: C, 77·75; H, 10·00. $C_{26}H_{40}O_3$ requires: C, 77·95; H, 10·07%).

9,19-*Cyclo*-4,4,14α-*trimethyl*-3β-*acetoxy*-5α,9β-*androstan*-17-*one* (VI)

(*a*) *By ozonolysis.* The olefin XV (0·206 g) in EtOAc (150 ml)–CCl_4 (15 ml) was ozonized at −10°. The crude "ozonide" after oxidative work-up[5] gave a complex product (0·2 g), which was chromatographed on SiO_2–gel/I (10 cm × 2 cm): (i) light petroleum (50 ml × 4), 0·01 g, rejected; (ii) 10% C_6H_6 in light petroleum (100 ml × 5), 0·115 g, semisolid. Fraction (ii) was further purified by rechromatography on SiO_2–gel/I (13 cm × 2 cm) to finally give after crystallization (Aqueous MeOH) pure VI, m.p. 162–163°, $[\alpha]_D$ +107° (*c*, 1·2%). Mass: *m/e* 372 (M^+; 13%), 43 (100%), 312 (71%), 269 (71%), 297 (67%), 122 (62%), 243 (37%), 91 (36%), 107 (34%), 55(33%), 81 (31%). (Found: C, 77·76; H, 10·10. $C_{24}H_{36}O_3$ requires: C, 77·37; H, 9·74%).

(*b*) *By hydroxylation*–$Pb(OAc)_4$ *cleavage.* A mixture of XV (0·5 g), OsO_4 (0·31 g), pyridine (0·195 g), ether (15 ml) and light petroleum (15 ml) was refluxed (40 hr) and solvent flashed off. The residual osmate ester was taken up in benzene (100 ml) and treated with H_2S[22] and then worked up to yield a product (0·53 g), which was chromatographed on SiO_2–gel/I (28 cm × 2·5 cm): (i) 25% C_6H_6 in light petroleum (350 ml), 0·135 g (XV), m.p. 146–148°; (ii) 50% EtOAc in C_6H_6 (50 ml × 5), 0·32 g required diol mixture, m.p. 109–120°. Fraction (ii) (0·233 g) in benzene (30 ml) was stirred (2 hr) with $Pb(OAC)_4$[23] (0·244 g) and neutral portion (0·21 g) chromatographed on SiO_2–gel/I (6·2 cm × 2 cm) and the main fraction (0·135 g, m.p. 152–161°) recrystallized from aqueous MeOH to give VI (m.p. 162–163°).

Isomerization of cycloartenyl acetate with N-*lithioethylenediamine and subsequent cleavage of products*

Cycloartenylacetate (1·5 g) was added in one lot to a stirred soln of N-lithioethylenediamine complex (Li 1·5 g, $NH_2.CH_2.CH_2.NH_2$ 45 ml; N_2) at 120–125° (bath temp) and the mixture maintained at this temp for 15 hr. The product obtained after usual work-up was acetylated (pyridine–Ac_2O) to give a product (1·47 g) shown by TLC ($AgNO_3$–silica gel; solvent: 30% C_6H_6 in hexane, two irrigations, 14·5 cm each) to be mixture of at least three compounds (R_f 0·51, 0·45, 0·38).

3β-*Acetoxy-cycloart*-17(20)-*ene* (XVI). The above mixture of olefins (0·866 g), OsO_4 (0·47 g), pyridine (0·3 g), light petroleum (20 ml) and ether (20 ml) was gently refluxed (1 week) and solvent flashed off. The residual osmate ester was taken up in benzene (200 ml), treated with H_2S and then worked up to yield a product (0·96 g), which was chromatographed on SiO_2–gel/I (43 cm × 1·5 cm): (i) 20% C_6H_6 in light petroleum (200 ml × 6), 0·32 g, m.p. 43–47°; (ii) EtOAc (100 ml × 5), 0·44 g a mixture of diols.

Fraction (i) was crystallized from aqueous EtOH to afford XVI, m.p. 47–49°, $[\alpha]_D$ + 30·8° (*c*, 1·3%). (Found: C, 81·36; H, 11·20. $C_{32}H_{52}O_2$ requires: C, 81·99; H, 11·80%).

$Pb(OAc)_4$ *cleavage of fraction* (ii). Fract. (ii) (0·44 g) in benzene (50 ml) was stirred (2 hr) with $Pb(OAc)_4$ (0·47 g) and the neutral fraction (0·37 g) chromatographed on SiO_2–gel/I (52 cm × 1·5 cm): (i) 80% C_6H_6 in light petroleum (250 ml), V (61 mg), m.p. 148–151°; (ii) benzene (200 ml), VI (40 mg), m.p. 152–160°.

Fract. (i) was crystallized from MeOH–Ether to furnish pure V, m.p. 153–154°.

Fract. (ii), was crystallized from aqueous MeOH to give pure VI, m.p. 162–163°.

24-*Methyl*-9,19-*cyclolanost*-24-*en*-3β-*ol* (XVIII)

Cyclolaudenol (5·0 g) was added to a stirred soln of N-lithioethylenediamine complex (Li 1·5 g, $NH_2.CH_2.CH_2.NH_2$ 45 ml; N_2) at 120–125° (bath temp) and the mixture maintained at this temp for 6 hr.

The product (4·61 g, m.p. 144–147°), thus obtained by usual work-up, on crystallization from MeOH–ether gave XVIII, m.p. 155–156°, $[\alpha]_D$ +56° (*c*, 0·8%); IR: OH 3420 cm^{-1}. (Found: C, 84·30; H, 11·70. $C_{31}H_{52}O$ requires: C, 84·50; H, 11·90%).

Acetate (pyridine–Ac_2O), m.p. 169–171°, $[\alpha]_D$ +73° (*c*, 1·3%); IR: —$OCOCH_3$ 1740,1245 cm^{-1}. (Found: C, 82·24; H, 11·28. $C_{33}H_{54}O_2$ requires: C, 82·1; H, 11·3%).

3β-*Acetoxy*-9,19-*cyclo*-25,26,27-*trisnor-lanost*-24-*one* (XIX)

The above acetate (5·0 g) was ozonized in dry $CHCl_3$ (250 ml) at −10°. The crude ozonide was decomposed by refluxing (2 hr) with water (50 ml). The product (4·8 g) obtained after usual work-up was chromatographed on SiO_2–gel/I (45 cm × 3 cm), and the major fraction (4·1 g, m.p. 152–156°) eluted with 10% ether in C_6H_6 (350 ml), was crystallized from MeOH when it furnished the known[20] XIX, m.p. 163–166°, $[\alpha]_D$ +86° (*c*, 0·65%); IR: C=O 1705, 1735 cm^{-1}; PMR: cyclopropane methylene (a pair of d centred at 0·35 and 0·56 ppm, $J = 5$ Hz); quaternary Me's at 0·85, 0·85, 0·88 and 0·96 ppm; —$COCH_3$ (3H, s at 1·96 ppm); —$OCOCH_3$ (3H, s at 2·05 ppm); —CH—OAc (1H, m centred at 4·46 ppm). (Found: C, 79·14; H, 10·59. $C_{30}H_{48}O_3$ requires: C, 78·89; H, 10·59%) (Lit.[20]: m.p. 170°, $[\alpha]_D$ +58°).

NaOBr *oxidation of* XIX. The trisnor-ketone XIX (5·0 g) in dioxan (550 ml) was introduced rapidly with stirring into a freshly prepared soln of NaOBr[24] (175 ml). After stirring for 6 hr at room temp (~25°) the product was worked up in the usual way and hydrolyzed (10% EtOH–KOH, 4 hr, reflux). The hydroxy-acid (IX; 4·8 g) thus obtained was acetylated (pyridine–Ac_2O) to afford after crystallization (MeOH) the known VII, m.p. 215–217, $[\alpha]_D$ +44·6° (*c*, 1·2%); IR: C=O 1700, 1740 cm^{-1} (Lit.[6]: 221·5–223°, $[\alpha]_D$ + 62°).

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