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Decomposition Reaction of Tosylhydrazones of Steroidal 2α,5α-Epoxy-3-ketones with Base[1]

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Decomposition reaction of 2α,5-epoxy-5α-cholestan-3-one tosylhydrazone (**1b**) and the 17β-acetoxyandrostane analogue (**1d**) with lithium hydride in toluene or xylene yielded the corresponding 1β,3β-cyclo-2α,5α-epoxy derivatives (**2a** and **2b**) comprising a 3-oxatricyclo[2.2.1.$0^{2,6}$]heptane system. The structure of **2a**, assumed from its spectral properties, was evidenced by the results of its catalytic hydrogenation providing the reductive cleavage products of the C_1–C_3 and the C_2–C_3 bond.

It is well known that the Bamford–Stevens reaction[3] of camphor tosylhydrazone gives rise to camphene and 1,7,7-trimethyltricyclo[2.2.1.$0^{2,6}$]heptane, an insertion product at C_6-H.[4] In the course of studies on steroidal transannular 2,5-epoxides, we have obtained 3-oxo-2α,5α-epoxides[5] possessing the 7-oxabicyclo[2.2.1]heptane system. Because of their structural resemblance, it was thought that these compounds may also undergo a similar type of reaction affording a 3-oxatricyclo[2.2.1.$0^{2,6}$]heptane derivatives.[6] On the other hand, interesting fragmentation reactions of steroidal 3-oxo-4,5-epoxides and other α,β-epoxyketones with tosylhydrazine leading to 4,5-seco-3-yn-5-ones, have been reported independently by two groups,[7,8] and since our compounds, possessing α,β′-epoxyketone partial structures, have a certain resemblance to these compounds, similar fragmentations might take place.[9] These considerations prompted us to initiate this work.

When 2α,5-epoxy-5α-cholestan-3-one[5] (**1a**) and 17β-acetoxy-2α,5-epoxy-5α-androstan-3-one[5] (**1c**) were treated with tosylhydrazine, the corresponding tosylhydrazones (**1b** and **1d**) could be isolated in high yields, but in neither case were any fragmentation products obtained. Therefore we turned to a study of the Bamford–Stevens reaction of **1b** and **1d**. The tosylhydrazone (**1b**) on heating with lithium hydride[10] in toluene or xylene furnished the C_1–H insertion product (**2a**), 1β,3β-cyclo-2α,5α-epoxide, in high yield. A 3-oxatricyclo[2.2.1.$0^{2,6}$]-heptane system for **2a** was assumed from the following spectral data. Its near infrared (IR) measurement provided the overtone and combination bands due to cyclopropyl C-H streching vibrations at 8396, 6012, 5804 and 5708 cm^{-1}.[11] In the nuclear magnetic resonance (NMR)

1) This work is Part XXX of "Thiosteroids" by K. Takeda and T. Komeno. Part XXIX: M. Kishi and T. Komeno, *Tetrahedron*, **27**, 1527 (1971).
2) Location: *Fukushima-ku, Osaka.*
3) W. S. Bamford and T. S. Stevens, *J. Chem. Soc.*, **1952**, 4735.
4) J.W. Powell and M.C. Whiting, *Tetrahedron*, **7**, 305 (1959); P. Clarke, M.C. Whiting, G. Papenmeier, and W. Reusch, *J. Org. Chem.*, **27**, 3356 (1962); R.H. Shapiro, *Tetrahedron Letters*, **1966**, 3401.
5) T. Komeno, H. Itani, H. Iwakura, and K. Nabeyama, *Chem. Pharm. Bull.* (Tokyo), **18**, 1145 (1970).
6) To our knowledge, 3-oxatricyclo[2.2.1.$0^{2,6}$]heptane-1,7-dicarboxylic acid was reported only by N.S. Zfirov and Yu. K. Yurév, *Zu. Obsch. Khim.*, **35**, 1802 (1965); *idem*, *Chem. Abstr.*, **64**, 3449 (1966).
7) M. Tanabe, D.E. Crowe, R.L. Dehn, and G. Detre, *Tetrahedron Letters*, **1967**, 3739.
8) 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*, **50**, 2101 (1967).
9) Assuming a similar mechanism, the formation of 4,5-seco-3,4-dien-5-ones in the reaction would be expected.
10) L. Caglioti, P. Grasselli, and A. Selva, *Gazz. Chim. Ital.*, **94**, 537 (1964).
11) H. Tanida, Y. Hata, Y. Matsui, and I. Tanaka, *J. Org. Chem.*, **30**, 2259 (1965).

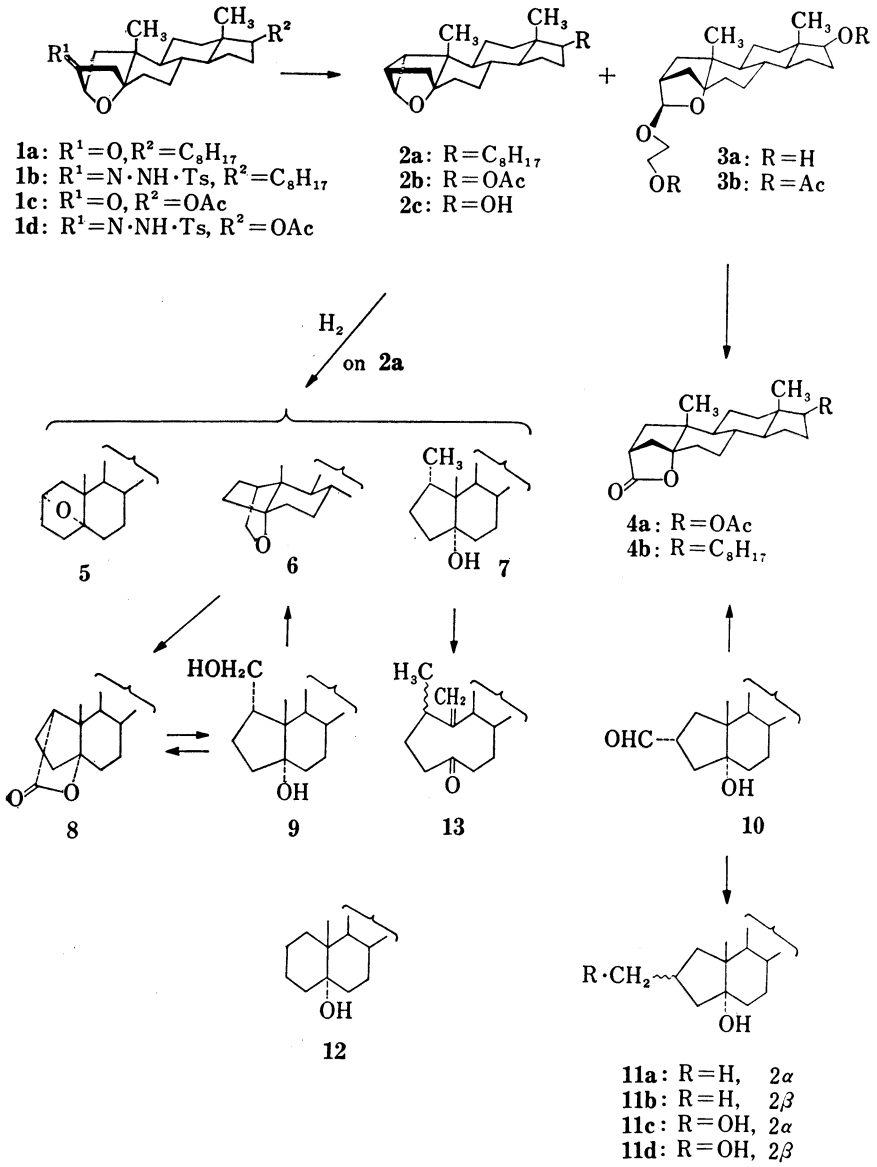

Chart 1

spectrum of **2a**, the proton on the carbon bearing an oxygen function resonates as a triplet at 6.25 τ, a considerably higher field than the range of 5.41—5.82 τ observed previously for the bridge head protons of 2α,5α-epoxy derivatives.[5] This shielding may be ascribed to the nature of a cyclopropyl proton.[12] The tosylhydrazone (**1d**) on heating with lithium hydride in a mixture of toluene and xylene[13] afforded the C_1-H insertion product (**2b**) in good yield. The structure for **2b** was assumed from the similarity of its spectral properties to those of **2a**.

12) N. S. Bhacca and D. H. Williams, "Application of NMR Spectroscopy in Organic Chemistry," Holden-Day Inc., San Francisco, London, and Amsterdam, 1964, p. 190.

13) The reaction of **1d** in toluene gave only the starting material, whereas the reaction of **1b** in toluene gave **2a** in 60.8% yield.

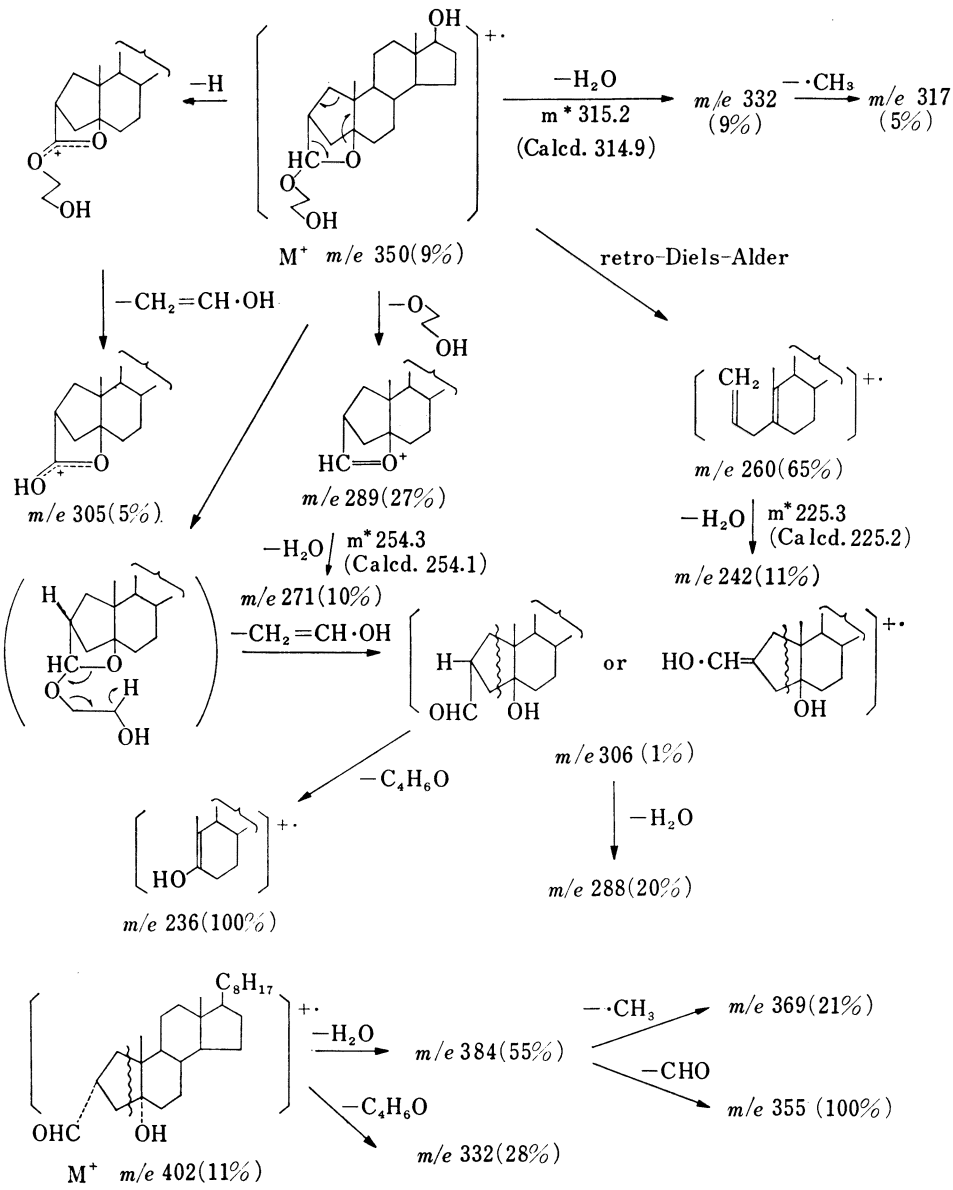

Chart 2

Heating **1d** with sodium dissolved in ethylene glycol in a steady stream of nitrogen gave a tricyclo-compound (**2c**) and a diol (**3a**) in 12% and 51% yield, respectively. Acetylation of **2c** gave the acetate, identical with the foregoing **2b**, which on treatment with lithium aluminum hydride (LAH) regenerated **2c**. The diol (**3a**), $C_{21}H_{34}O_4$, was characterized as a solvent insertion product with a rearranged skelton, 5,17β-dihydroxy-A-nor-5α-androstan-2α-yl aldehyde lactol 2'-hydroxyethyl ether, from the following evidences. The mass spectrum of **3a** showed a molecular ion (M^+) peak at *m/e* 350, a fragment due to retro-Diels–Alder decomposition at *m/e* 260 (M^+–90) and other fragment peaks reasonable for the assigned structure as seen in Chart 2. Acetylation of **3a** afforded an oily acetate (**3b**), the NMR spectrum of which

revealed the bridgehead proton signal at 7.70 τ as a doublet (J=4.5 Hz), a multiplet corresponded to four protons at 5.7—6.5 τ as an A_2B_2 pattern assignable to an O–CH_2–CH_2–O moiety and a singlet at 5.63 τ due to a proton on the carbon bearing oxygen functions, supporting the exo configuration of the substituent in **3b**. Jones oxidation of **3b** in the presence of silver chromate[14] furnished a γ-lactone (**4a**) ($\nu_{C=O}$ 1777 cm^{-1}), whose circular dichroism (CD) curve showed a negative n–π^* Cotton effect, consistent with the prediction from the lactone sector rule[15] and also in agreement with that of 5-hydroxy-A-nor-5α-cholestan-2α-yl carboxylic acid lactone (**4b**) prepared previously.[16] Hence, the structures for **4a** and also **3a** were established as described above. These results from the decomposition reaction of the tosylhydrazones (**1b** and **1d**) with base are considered to be in line with those observed in other systems.[17] The reaction of **1b** or **1d** with base in aprotic solvents afforded the C-H insertion product, although it is not fully understood what kind of species is involved as the reaction intermediate, a "hot" carbonium ion or a carbene. With regard to the formation of the main product, **3a**, it is unequivocal that in a protic medium, a carbonium ion generated from the diazoalkane rearranges in a Wagner–Meerwein or a concerted manner to a carbonium ion stabilized by the adjacent oxygen participation, which in turn suffers nucleophilic attack by a molecule of the solvent from the less hindered exo side.

Chemically decisive proof for the tricyclo structure of **2a** was gained from the results of its catalytic hydrogenation in the presence of Adams catalyst in acetic acid, providing three products. Among them, the compound (**5**), formed in the lowest yield (4.9%), was readily identified as 2α,5-epoxy-5α-cholestane[5] by direct comparison with an authentic sample. This indicates the occurrence of reductive fission of the C_1–C_3 bond in the reaction. The major product (**6**), formed in 59% yield, was characterized as a dihydro compound, containing a tetrahydrofuran ring fused at C_1 and C_5, and arising from the reductive cleavage of the C_2-C_3 bond. Ruthenium tetroxide oxidation[18] of **6** gave a γ-lactone (**8**) ($\nu_{C=O}$ 1797 cm^{-1}) in 85% yield, whose CD curve, different from those of **4a** and **4b**, exhibited a positive n–π^* Cotton effect indicative of the presence of the C_1-carboxylic acid moiety based on the lactone sector rule.[15] The third component (**7**), formed in 23.5% yield, was characterized as a tetrahydro compound carrying a hydroxyl group from its elemental analysis and spectral properties. The hydroxyl group showed a resistance to acetylation indicative of a tertiary hydroxyl. This was further supported by the mass spectrum of **7**, in which the M^+ peak was observed at m/e 388 and other major fragment peaks were found to correspond to those of 5α-cholestane minus two hydrogen atoms. Among the three possible structures for **7**, 5α-cholestan-5-ol (**12**), 2α-methyl-A-nor-5α-cholestan-5-ol (**11a**) and 1α-methyl-A-nor-5α-cholestan-5-**ol, the** first two could be excluded by the direct comparison with their authentic samples. The 2α-methyl compound (**11a**) was prepared by Huang-Minlon reduction of 5-hydroxy-A-nor-5α-cholestan-2α-yl aldehyde[16] (**10**) accompanied by a small amount of the 2β-methyl compoumd (**11b**). The configuration at C_2 in **11a** and **11b** were evidenced by the chemical shifts of the C_{10}-methyl signals in their NMR spectra. A similar preference for the product with retained configuration was also observed in LAH reduction of **10**, which afforded a mixture of 2α-hydroxymethyl-A-nor-5α-cholestan-5-ol (**11c**) and the 2β-epimer (**11d**) in a ratio of 4: 1. The structure for **11c** was established by its IR spectrum in a CCl_4 solution, showing the intramolecularly hydrogen-bonded hydroxyl absorption band at 3591 cm^{-1} (*cf.* 3616 cm^{-1} for **11d**). As a result, the remaining structure, 1α-methyl-A-nor-5α-cholestan-5-ol, was assumed for **7**

14) Ch. Meystre, K. Heusler, J. Kalvoda, P. Wieland, G. Anner, and A. Wettstein, *Helv. Chim. Acta*, **45**, 1317 (1962).
15) J.P. Jennings, W. Klyne, and P.M. Scopes, *Proc. Chem. Soc.*, **1964**, 412; *J. Chem. Soc.*, **1965**, 7211, 7229; G. Snatzke, H. Ripperger, Chr. Horstmann, and K. Schreiber, *Tetrahedron*, **22**, 3103 (1966).
16) T. Tsuji, T. Komeno, H. Itani, and H. Tanida, *J. Org. Chem.*, *in Press*.
17) D. N. Kirk and M. P. Hartshorn, "Steroid Reaction Mechanisms," Elsevier Publishing Co., Amsterdam, London, New York, 1968, pp. 339—342.
18) M.E. Wolff, J.F. Kerwin, F.F. Owings, R.B. Lewis, and B. Blank, *J. Org. Chem.*, **28**, 2729 (1963).

although this could not be fully established because of the failure of the interconversion between **6** and **7**. An attempt to prepare **7** from **6** was unsuccessful: LAH reduction of the γ-lactone (**8**) derived from **6** gave 1α-hydroxymethyl-A-nor-5α-cholestan-5-ol (**9**), which on treatment with tosyl chloride in pyridine afforded the parent tetrahydrofuran (**6**) and no monotosylate was obtained. Oxidation of **9** with pyridine–chromic anhydride complex regenerated the lactone (**8**) and no hydroxyaldehyde was formed. Attempted conversion of **7** into **6** by reaction with lead tetra-acetate in the absence or presence of iodine[19] in cyclohexane failed, instead, a ketone (**13**) ($\nu_{C=O}$ 1708 cm^{-1}) was isolated as an amorphous substance. In its NMR spectrum, in addition to the three protons singlet due to the C_{13}-methyl group, the secondary methyl protons resonate at 8.98 τ as a doublet and two vinyl protons assignable to an exo methylene group at 5.17 and 5.00 τ as a pair of doublets, indicating that the fragmentation reaction had taken place to yield a 9-membered ketone. Though this is an undesired product, the presence of 5-hydroxyl group in **7** is suggested, since similar reactions have been observed in lead tetra-acetate oxidation of 5α-cholestan-5-ol derivatives.[20]

Experimental[21]

2α,5-Epoxy-5α-cholestan-3-one Tosylhydrazone (1b)——A stirred mixture of 2.79 g of **1a**,[5] 80 ml of AcOH and 3.2 g of $TsNHNH_2$ was warmed at 50° for 3.5 hr. After cooling, the mixture was poured into ice–water and extracted with a mixture of ether and CH_2Cl_2 (2:1). The organic layer was washed successively with water, 10% Na_2CO_3 and water, dried over Na_2SO_4 and evaporated to dryness leaving solids. Recrystallization from CH_2Cl_2–MeOH afforded 3.762 g (94.8%) of **1b**, mp 194—196°, $[\alpha]_D^{20}$ +51.9±1.1° (c=0.832). IR ν_{max} cm^{-1}: 3208, 1694, 1597, 1334, 1167, 924, 815. UV λ_{max}^{MeOH} mμ (ε): 274 (780), 229 (13850). NMR τ: 9.35 (18-H), 9.13 (19-H), 7.58 (Ts-Me), 5.41d (2β-H, $J_{2\beta:1\alpha}$=6.0 Hz), an A_2B_2 pattern centred at 2.45 τ (C_6H_5-H). *Anal.* Calcd. for $C_{34}H_{52}O_3N_2S$: C, 71.78; H, 9.21; N, 4.93; S, 5.64. Found: C, 71.84; H, 9.13; N, 4.93; S, 5.62.

The reaction of **1a** with excess of $TsNHNH_2$ in boiling EtOH gave the same result and **1b** was obtained.

17β-Acetoxy-2α,5-epoxy-5α-androstan-3-one Tosylhydrazone (1d)——A mixture of 486 mg of **1c**, 20 ml of AcOH and 392 mg of $TsNHNH_2$ was allowed to stand at room temperature for 2 days. After dilution with ice water, extraction with CH_2Cl_2 gave 770 mg of **1d**, as an amorphous material, which could not be crystallized from any solvent and showed absorption bands characteristic of a tosylhydrazone moiety in the IR spectrum. $\nu_{max}^{CHCl_3}$ cm^{-1}: 3200, 1726, 1597, 1340, 1117.

1β,3β-Cyclo-2α,5-epoxy-5α-cholestane (2a)——A stirred mixture of 489 mg of **1b** and 3.86 g of finely powdered LiH in 60 ml of a mixture of toluene and xylene (1:1) was heated under reflux for 24 hr. After cooling, the mixture was diluted with ether and the excess of LiH was filtered off. The filtrate, combined with the ether washings of the LiH, was washed with 10% Na_2CO_3 and water, and dried over Na_2SO_4. Evaporation of the solvent left 350 mg of residue which was dissolved in petroleum ether and chromatographed over 10.4 g of neutral Al_2O_3 (grade III). The fractions eluted with the solvent gave 273 mg (80.7%) of **2a**. Recrystallization from acetone afforded the pure sample, mp 128—129°, $[\alpha]_D^{22}$ 0 (c=0.960). IR ν_{max} cm^{-1}: 3080, 3060, 1156, 1012, 993, 963, 949, 882, 798, 788, Near IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2ν (overtone), 6012 (ε 0.871); 3ν, 8396 (ε 0.327); combination band, 5708 (ε 1.212), 5804 (ε 1.334), 7246 (ε 0.28). NMR τ: 9.35 (18-H), 9.17 (19-H), 6.25 t (2β-H, J=4.0 Hz). *Anal.* Calcd. for $C_{27}H_{44}O$: C, 84.31; H, 11.53; mol. wt., 384.62. Found: C, 84.53; H, 11.47; mol. wt. (osmometer, $CHCl_3$), 383.

A mixture of 1.70 g of **1b** and 5.2 g of LiH in 70 ml of xylene was heated for 1.5 hr and the same treatment as described above afforded 871 mg (72.5%) of **2a**. A mixture of 102 mg of **1b** and 300 mg of LiH in

19) K. Heusler and J. Kalvoda, *Angew. Chem. Intern. Ed. Engl.*, **3**, 525 (1964); K. Heusler, *Tetrahedron Letters*, **1964**, 3975.

20) M. Akhtar and S. Marsh, *Tetrahedron Letters*, **1964**, 2475; M. Lj. Mihailović, M. Stefanović, Lj. Lorenć, and M. Gašić, *ibid.*, **1964**, 1867; D. Rosenthal, C, F. Lefler, and M. E. Wall, *ibid.*, **1965**, 3203.

21) All melting points were measured on a Kofler hot-stage apparatus and are uncorrected. Optical rotaions were determined in 1% EtOH–$CHCl_3$ solution with a Perkin Elmer Polarimeter, type 141. Unless otherwise stated IR spectra were recorded in Nujol mulls with a Koken DS-201B spectrophotometer. Intramolecular hydrogen bonding was measured in about 1.5×10^{-3} M CCl_4 solution using a 20 mm cell. Mass spectra were observed with a Hitachi RMU-6 mass spectrometer using an ionizing voltage of 70 eV. Samples were introduced by a direct inlet probe. Unless otherwise stated, NMR were taken on $CDCl_3$ solutions with a Varian-A-60 spectrometer, TMS serving as internal standard. For preparative thin-layer chromatography (TLC) Silica gel G (E. Merck Co.) was used as an absorbent.

6.5 ml of toluene was refluxed for 4.5 hr and the same treatment as described above gave 42 mg (60.8%) of **2a**.

17β-Acetoxy-1β,3β-cyclo-2α,5-epoxy-5α-androstane (2b)——A stirred mixture of 2.30 g of **1d** and 2.0 g of LiH in 60 ml of a mixture of toluene and xylene (1:1) was refluxed for 1.5 hr. Working up in the same way as mentioned above gave 1.35 g of a crude material which was purified by chromatography over 30 g of Al_2O_3. Fractions eluted with petroleum ether–benzene (4:1—1:1) gave 846 mg (57.2%) of **2b**. Recrystallization from acetone–*n*-hexane afforded the pure sample, mp 165—167°, $[\alpha]_D^{22}$ −21.4±0.6° (c=0.991). IR ν_{max} cm^{-1}: 3085, 3071, 1732, 1249, 1059, 1045, 1023, 997, 962, 918, 884, 800, 789. NMR τ: 9.22 (18-H), 9.15 (19-H), 7.97 (AcO), 6.25 t (2β-H, J=4.0 Hz), 5.40 (17α-H). *Anal.* Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.20; H, 9.06.

17β-Hydroxy-1β,3β-cyclo-2α,5-epoxy-5α-androstane (2c)——To a solution of 6.8 g of Na in 150 ml of ethylene glycol was added a solution of 1.50 g of **1d** in 50 ml of the solvent. The solution was refluxed for 3 hr in a steady stream of N_2 and concentrated to about 100 ml. The resulting mixture was poured into ice-water and extracted with CH_2Cl_2. The CH_2Cl_2 solution was washed with 10% Na_2CO_3 and water and dried over Na_2SO_4. Evaporation of the solvent yielded 777 mg of a mixture, which showed two spots on TLC and was subjected to preparative TLC using cyclohexane–AcOEt (1:1) as developing solvent. The less polar fraction gave 103 mg (12.3%) of **2c**, which on recrystallization from *n*-hexane afforded the pure sample, mp 126—127°, $[\alpha]_D^{21}$ −21.6±1.1° (c=0.542). IR ν_{max} cm^{-1}: 3458, 3352, 3098, 3068, 1060, 1053, 1015, 990, 965, 952, 883, 805, 791. NMR τ: 9.29 (18-H), 9.15 (19-H), 6.36 (17α-H), 6.26 t (2β-H, J=4.0 Hz). *Anal.* Calcd. for $C_{19}H_{28}O_2 \cdot 1/2H_2O$: C, 76.72; H, 9.83. Found: C, 76.75; H, 9.85.

Treatment of 712 mg of **2b** with 100 mg of LAH in 24 ml of a mixture of ether and THF (1:1) for 2 hr at room temperature yielded 607 mg (97.8%) of **2c**, which was identified by mixed mp and comparison of IR spectrum. Acetylation of this compound with Ac_2O in pyridine at room temperature overnight gave an acetate identical with **2b**.

5,17β-Dihydroxy-A-nor-5α-androstan-2α-yl Aldehyde Lactol 2′-Hydroxyethyl Ether (3a)——The more polar fraction, separated in the preparative TLC of the above experiment, afforded 518 mg (50.8%) of **3a**. Recrystallization from acetone and *n*-hexane gave the pure sample, mp 163.5—166°, $[\alpha]_D^{21}$ −19.3±1.1° (c=0.534). IR ν_{max} cm^{-1}: 3616, 3466, 1087, 1075, 1062, 1052, 983, 967, 962, 925, 907, 882. NMR τ: 9.26 (18-H), 9.09 (19-H), *ca.* 6.32 m (17α-H, O·CH_2–CH_2–O and 2β-H), 5.63s (–O–$\dot{C}$H–O–, endo-H). *Anal.* Calcd. for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78. Found: C, 71.87; H, 9.79.

Acetylation of 518 mg of **3a** with 3 ml of Ac_2O in 9 ml of pyridine at room temperature overnight gave 645 mg of a diacetate (**3b**) as an amorphous substance which could not be crystallized from any solvent and showed one spot on TLC. NMR τ: 9.21 (18-H), 9.11 (19-H), 7.98 & 7.95 (OAc), 7.70 broad d (2β-H, J=4.5 Hz), 6.55—5.7 m (O·CH_2·CH_2–O), 5.63s (O–$\dot{C}$H–O, endo-H), 5.40 (17α-H).

5,17β-Dihydroxy-A-nor-5α-androstan-2α-yl Carboxylic Acid Lactone 17-Monoacetate (4a)——To a stirred mixture of 600 mg of **3b** and 60 mg of Ag_2CrO_4 in 6 ml of acetone was added 0.77 ml of 8 N Jones reagent.[22] The resulting mixture was stirred for 1 hr at room temperature. After addition of 150 ml of 3.5% aqueous AcONa solution, extraction with CH_2Cl_2 afforded 392 mg of a crude material, which showed two spots on TLC and was purified by preparative TLC (cyclohexane–AcOEt=2:1). It provided 62 mg (10.3%) of the starting material (**3a**) as the more mobile fraction and 270 mg (56.3%) of **4a** as the less mobile one. Recrystallization of the latter from *n*-hexane afforded the pure sample, mp 156—157.5°, $[\alpha]_D^{22}$ −12.4±0.9°, (c=0.565). IR ν_{max} cm^{-1}: 1777, 1732, 1253, 1084, 1058, 1043, 1025, 915, 898, 877, 724. CD (iso-octane) [θ] (mμ): 0 (252), −12390 (218), −3575 (200). NMR τ: 9.19 (18-H), 8.92 (19-H), 7.97 (OAc), 7.26 m (2β-H, $w^1/_2$h=6.0 Hz), 5.40 (17α-H). *Anal.* Calcd. for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.84; H, 8.72.

Catalytic Hydrogenation of 1β,3β-Cyclo-2α,5-epoxy-5α-cholestane (2a)——a) The tricyclocompound (**2a**) (101 mg) was hydrogenated in the presence of prereduced PtO_2 (150 mg) in 4.5 ml of a mixture of AcOH and ether (1:7) for 30 min at room temperature. After removal of the catalyst, the product was extracted with ether to give 107 mg of a mixture showing four spots on TLC. The products were separated by preparative TLC (benzene) affording 24 mg (23.5%) of **7**, 3 mg (3.0%) of the starting material (**2a**), and 66 mg of a mixture of **5** and **6** in order of their decreasing mobility.

Recrystallization of **7** from MeOH afforded the pure sample, mp 79.5—80°, $[\alpha]_D^{24}$+56.5±1.0° (c=1.003). IR ν_{max} cm^{-1}: 3436, 991, 975, 932, 912. NMR τ: 9.31 (18-H), 9.18 (19-H); (in C_6D_6): 9.30 (18-H), 9.27 (19-H). Mass Spectrum *m/e*: 388 [M^+] (3%), 370 [M^+–H_2O] (57%), 355 [M^+–(H_2O+CH_3)] (32%), 215 [$C_{16}H_{24}$] (33%), 214 [$C_{16}H_{23}$] (19%), 147 [$C_{11}H_{16}$] (26%), 108 [base peak]. *Anal.* Calcd. for $C_{27}H_{48}O$: C, 83.44; H, 12.45. Found: C, 83.59; H, 12.55.

The mixture of **5** and **6** was separated by preparative TLC using a double development method (benzene: cyclohexane=10:1). The more mobile fraction gave 5 mg (4.9%) of **5**, mp 101.5—102°, which was identified by mixed mp and comparison of the IR spectrum. The less mobile fraction afforded 60 mg (59.1%) of **6**, which upon recrystallization from ether–acetone gave the pure sample, mp 130—131°, $[\alpha]_D^{24}$+34.8±1.4° (c=0.546). IR ν_{max} cm^{-1}: 997, 973, 943, 915. NMR τ: 9.32 (18-H), 9.09 (19-H), 6.59 d, 6.13 dt (O-CH_2-,

22) C. Djerassi, R.R. Engle, and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).

endo-H & exo-H, $J_{gem}=7.0$, $J_{vic}=3.0$ Hz). *Anal.* Calcd. for $C_{27}H_{46}O$: C, 83.87; H, 11.99. Found: C, 83.87; H, 11.93.

b) In another run, 200 mg of **2a** was hydrogenated in the presence of 300 mg of prereduced PtO_2 in 9 ml of a mixture of AcOH and ether (1:7) for 3 hr at room temperature. After work up, preparative TLC of the product gave 77 mg (38.1%) of **7** and 100 mg (49.7%) of **6**.

5-Hydroxy-A-nor-5α-cholestan-1α-yl Carboxylic Acid Lactone (8)——a) To 30 ml of a cooled solution of RuO_4 in CCl_4, generated from 417 mg of RuO_2 and 3.0 g of $NaIO_4$ according to Nakata's method,[23] was added 82 mg of **6**. The resulting mixture was stirred for 5 hr under cooling with ice water and allowed to stand overnight in a refrigerator. To the mixture 8 ml of ether was added and the deposited RuO_2 was filtered off. The filtrate was washed with 10% Na_2CO_3 and water and dried over Na_2SO_4. Evaporation of the solvent gave 100 mg of a crude material, which was purified by preparative TLC (benzene) affording 72 mg (84.8%) of **8**. Recrystallization from MeOH yielded the pure sample, mp 122—123.5°, $[\alpha]_D^{24}+38.3\pm0.8°$ ($c=0.983$). IR ν_{max} cm^{-1}: 1797, 1206, 1125, 1020, 998, 913. CD (iso-octane) [θ] (mμ): O (240), +2876 (220), +1397 (208). NMR τ: 9.33 (18-H), 9.09 (19-H), 7.43d (1β-H, $J=2.5$ Hz). *Anal.* Calcd. for $C_{27}H_{44}O_2$: C, 80.94; H, 11.07. Found: C, 80.70; H, 11.10.

b) A mixture of 124 mg of **9** and 104 mg of CrO_3 in 2 ml of pyridine was stirred at room temperature for 8 hr and poured into ice water. Extraction with ether–CH_2Cl_2 (9:1) afforded 125 mg of a crude material, which was purified by preparative TLC (cyclohexane: AcOEt=4:1) giving 105 mg of **8**. Recrystallization from MeOH gave 87 mg of the pure sample, which was identified by mixed mp and comparison of the IR spectrum.

1α-Hydroxymethyl-A-nor-5α-cholestan-5-ol (9)——To a stirred suspension of 39 mg of LAH in 1 ml of dry ether a solution of 104 mg of **8** in 3 ml of dry ether was added. The resulting mixture was stirred for 1 hr at room temperature and worked up in the usual way. Recrystallization of the product from CH_2Cl_2–acetone afforded 78 mg (74.2%) of **9**, mp 166.5—169°, $[\alpha]_D^{23}+38.6\pm0.9°$ ($c=0.854$). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3637, 3602, 3435; ν_{max} cm^{-1}: 3160, 1122, 1002. NMR τ: 9.32 (18-H), 9.11 (19-H), 6.63—6.07 broad AB type q (-CH_2-O, $J_{AB}=11.0$ Hz). *Anal.* Calcd. for $C_{27}H_{48}O_2$: C, 80.14; H, 11.96. Found: C, 80.08; H, 11.88.

Treatment of 127 mg of **9** with 85 mg of Ts-Cl in 2 ml of pyridine at room temperature for 2 days, followed by separation by preparative TLC (cyclohexane: AcOEt=4:1) afforded 48 mg (39.7%) of **6** and 57 mg (44.8%) of the starting material (**9**).

Lead Tetraacetate Oxidation of 1α-Methyl-A-nor-5α-chloestan-5-ol (7)——a) A mixture of 23 mg of **7**, 36 mg of $CaCO_3$ and 120 mg of $Pb(OAc)_4$ in 2.8 ml of cyclohexane was refluxed for 4 hr. After cooling the excess of $CaCO_3$ and $Pb(OAc)_4$ was filtered off and washed with ether. The combined filtrate was washed with 10% Na_2CO_3 and water and dried over Na_2SO_4. Evaporation of the solvent gave 22 mg of an oily mixture, which was purified by preparative TLC (benzene) affording 6 mg (26.1%) of the starting material (**7**) as the mobile fraction and 10 mg (43.7%) of **13** as the less mobile one. Crystallization of **13** was unsuccessful and **13** showed the following spectral properties. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3060, 1708, 1639, 916, 893. UV λ_{max}^{MeOH} mμ (ε): 275 (50). CD (MeOH) [θ] (mμ): O (330), −3339 (290), O (247), +35980 (206); (iso-octane): O (330), −1021 (322), −1560 (312), −2469 (308), −3254 (302), −2988 (294), O (257), +51840 (205), +35460 (200). NMR τ: 9.32 (18-H), 5.17d, 5.00d (exo=C$\underline{H}_2$, $J=1.8$ Hz), 8.98d (1α-CH_3, $J=6.2$ Hz); (in C_6D_6): 9.36 (18-H), 5.23d, 5.03d (exo=C$\underline{H}_2$, $J=1.8$ Hz), 9.01d (1α-CH_3, $J=6.4$ Hz).

b) A mixture of 24 mg of **7**, 20 mg of I_2, 37 mg of $CaCO_3$ and 120 mg of $Pb(OAc)_4$ in 3.2 ml of cyclohexane was refluxed for 3 hr under irradiation with a 100 W lamp. Work up in the same way as described in a) gave 28 mg of an oil, which was purified by preparative TLC (benzene) affording 13 mg (54.3%) of an oily substance identical with **13**.

Huang-Minlon Reduction of 5-Hydroxy-A-nor-5α-cholestan-2α-yl Aldehyde (10)——A mixture of 122 mg of **10**, 285 mg of KOH and 1.7 ml of 80% $NH_2NH_2\cdot H_2O$ in 10 ml of triethylene glycol was refluxed at 130° for 1.5 hr then distilled until the inner temperature reached at 200°. The remaining mixture was heated at the same temperature for 1.5 hr. After cooling, the mixture was poured into ice water and extracted with ether. The ethereal solution was worked up in the usual manner to give 118 mg of a mixture, which was separated by preparative TLC using benzene: *n*-hexane (4:1). The more mobile fraction gave 84 mg (71.3%) of **11a**, which upon recrystallization from MeOH afforded the pure sample, mp 104—104.5°, $[\alpha]_D^{25}+16.2\pm0.6°$ ($c=1.010$). IR ν_{max} cm^{-1}: 3607, 3446, 951. NMR τ: 9.34 (18-H), 9.16 (19-H); (in C_6D_6): 9.30 (18-H), 9.22 (19-H), 8.82d (2α-CH_3, $J=7.0$ Hz). *Anal.* Calcd. for $C_{27}H_{48}O$: C, 83.43; H, 12.45. Found: C, 83.34; H, 12.40.

The less mobile fraction gave 33 mg (26.5%) of **11b**, which was recrystallized from MeOH yielding the pure sample, mp 106—106.5°, $[\alpha]_D^{25}+16.7\pm0.6°$ ($c=1.021$). IR ν_{max} cm^{-1}: 3614, 3480, 953, 946. NMR τ: 9.34 (18-H), 9.10 (19-H); (in C_6D_6): 9.30 (18-H), 9.17 (19-H), 8.91d (2β-CH_3, $J=7.0$ Hz). *Anal.* Calcd. for $C_{27}H_{48}O$: C, 83.43; H, 12.45. Found: C, 83.19; H, 12.40.

LAH Reduction of 5-Hydroxy-A-nor-5α-cholestan-2α-yl Aldehyde (10)——The aldehyde (**10**) (332 mg) was reduced with 122 mg of LAH in 11 ml of dry ether at room temperature. After work up in the usual

23) H. Nakata, *Tetrahedron*, **19**, 1959 (1963).

manner, the product (334 mg) was separated by preparative TLC (cyclohexane: AcOEt=1:1). The less polar fraction gave 240 mg (72.0%) of **11c**, which upon recrystallization from ether–*n*-pentane afforded the pure sample, mp 117—118°, $[\alpha]_D^{23}+142\pm0.5°$ ($c=1.055$). IR $\nu_{OH}^{CCl_4}$ cm^{-1}: 3648, 3591; ν_{max} cm^{-1}: 3271, 1048, 980, 970, 955, 857. NMR τ: 9.33 (18-H), 9.09 (19-H), 6.17 (2α-C**H$_2$**–OH). *Anal.* Calcd. for $C_{27}H_{48}O_2$: C, 80.14; H, 11.96. Found: C, 79.93; H, 11.93. The more polar fraction yielded 62 mg (18.6%) of **11d**, which was recrystallized from CH_2Cl_2–MeOH to give the pure sample, mp 165.5—166°, $[\alpha]_D^{23}+17.8\pm1.3°$ ($c=0.438$). IR $\nu_{OH}^{CCl_4}$ cm^{-1}: 3631, 3616; ν_{max} cm^{-1}: 3336, 1049, 1042, 948, 869. NMR τ: 9.33 (18-H), 9.08 (19-H), 6.38 (2β-CH_2–OH). *Anal.* Calcd. for $C_{27}H_{48}O_2\cdot{}^1/_2H_2O$: C, 79.25; H, 11.96. Found: C, 79.27; H, 11.82.

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