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REDUCTION OF STEROIDAL DICARBONYL COMPOUNDS WITH POLY(*N*-ISOPROPYLIMINOALANE)

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Abstract—Reduction of 6,17- and 6,20-dioxo-3α,5-cyclo-5α-steroids with poly(N-isopropyliminoalane) $(HAlN\text{-}i\text{-}Pr)_6$ yields 6α-hydroxyketones as the major products. The unexpected reduction outcome observed in the case of some steroidal ketoaldehydes is discussed. Treatment of methyl lithocholate **16** and methyl 3β-hydroxy-5α-etianate **18** with the same hydride is also reported.

We have previously reported[1] the selective reduction with poly(N-isopropyliminoalane) $(HAlN\text{-}i\text{-}Pr)_6$ of the 4-en-3-one group in the presence of a 17- or 20-keto group of some steroidal diketones.

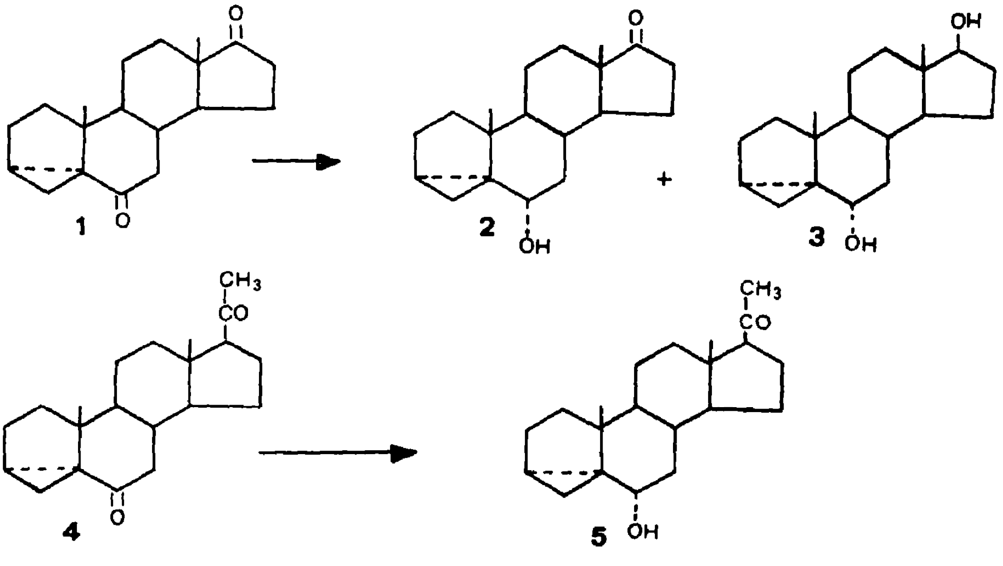
In this paper the results of the reaction of 6,17- and 6,20-dioxo-3α,5-cyclo-5α-steroids and of some steroidal ketoaldehydes with $(HAlN\text{-}i\text{-}Pr)_6$ are presented.

Reduction of both 3α,5-cyclo-5α-androstane-6,17-dione **1** and 3α,5-cyclo-5α-pregnane-6,20-dione **4** in aprotic solvents proceeded with remarkable regio- and stereo-selectivity to give the corresponding 6α-hydroxyketone as the main product. As shown in Scheme 1, reduction of **1** afforded together with 6α-hydroxy-3α,5-cyclo-5α-androstan-17-one **2** (55% yield), 3α,5-cyclo-5α-androstane-6α,17β-diol **3** (22% yield), while treatment of **4** gave 6α-hydroxy-3α,5-cyclo-5α-pregnan-20-one **5** (68% yield) as the only discernible reduction product.

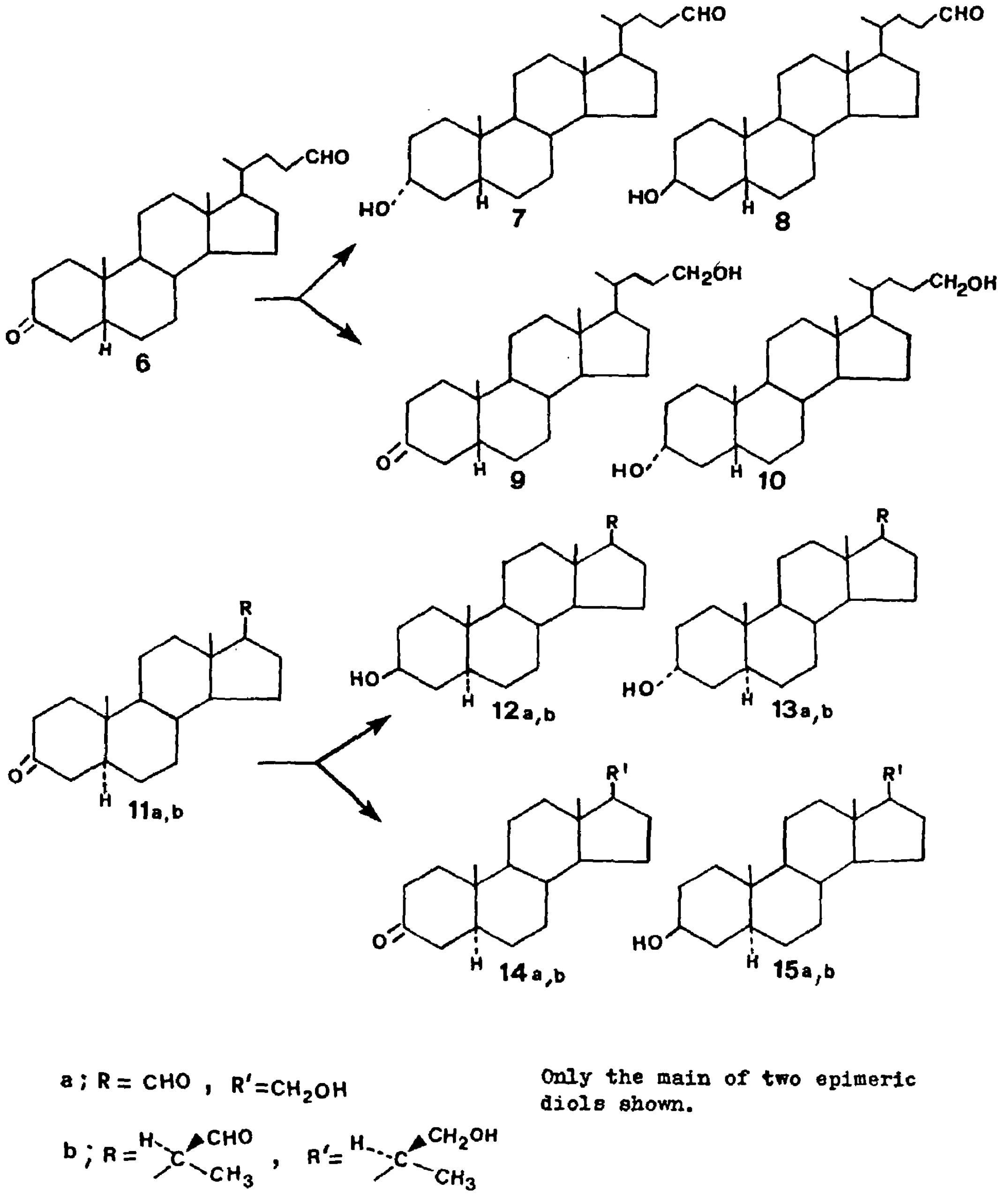
Configurational assignment to C-6 OH group in **2**,**5**, and **3** has been made on the basis of the position and resonance pattern (dd J = 4.5 and 11.5 Hz) of the C-6 proton according to Tadanier and Cole.[2] It is noteworthy that in both cases other monoreduction products could not be detected in the reaction mixtures. These results confirm that poly(N-isopropyliminoalane) is a reagent suitable for the selective reduction of several diketones in order to yield ketoalcohols sometimes[3] difficult to obtain by other ways.

Its application was then extended to some ketoaldehydes which were conveniently prepared by oxidation of the corresponding diols with Collins' reagent[4] under different reaction conditions.

As shown in Table 1 no appreciable selectivity was exhibited by $(HAlN\text{-}i\text{-}Pr)_6$ when the reaction was carried out on 3-oxo-5β-cholan-24-al **6**, 3-oxo-5α-



Scheme 1.



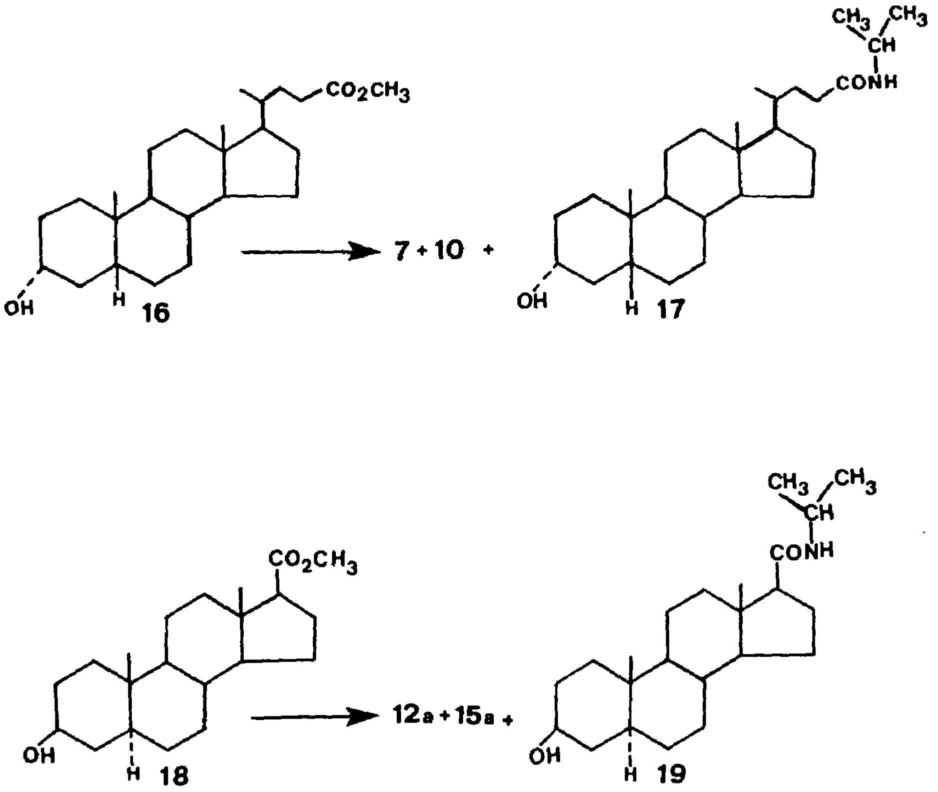
Only the main of two epimeric diols shown.

Scheme 2.

Table 1. Product distribution (%)

Ketoaldehyde	3αOH, CHO	3βOH, CHO	3-CO,CH$_2$OH	Diols	Start. mat. recovered
6	20	6	12	28	9
11a	5	16	22	27	10
11b	5	18	20	31	11

Yields were calculated by NMR analysis of chromatographic fractions.



Scheme 3.

androstane-17β-carboxaldehyde **11a**, and (20 *S*)-3-oxo-22,23-dinor-5α-cholan-24-al **11b**, since the corresponding diols were the main products. Besides, treatment of **6** with poly(N-isopropyliminoalane) afforded lithocholic aldehyde **7** as the major monoreduction product, while a slightly preferential reduction of the aldehydic group occurred with **11a** and an intermediate behaviour was exhibited by **11b**.

These product distributions are to be regarded as surprising in view of our previous hypothesis on steric hindrance as the main factor affecting the observed site-selectivity.[1] The preferred attack at the less hindered aldehydic group in **6**, **11a**, and **11b** would be expected to afford the corresponding ketoalcohols **9**, **14a**, and **14b** as the main reaction products. Furthermore, the selective reduction of aldehydes in the presence of ketones by bulky hydrides has been reported.[5] In this connection the observed decreasing ratios of 3-OH,CHO/3-CO,CH_2OH reaction products in the series **6**, **11b**, and **11a** (Table 1) disagree with a steric hindrance control. The aldehydic group of **6** is without doubt less hindered than those present in **11b** and **11a**.

This unexpected reduction outcome may be rationalised by assuming that a concurrent formation of imines, arising from an attack of the isopropylamine on the aldehydic group of ketoaldehydes, can occur. These iminic derivatives, not reduced by poly(N-isopropyliminoalane), would be then hydrolysed during the chromatographic separation on silica (plc). This hypothesis which accounts for the obtained products distributions is supported by the absence of the characteristic low field aldehydic signal in the ^{1}H NMR spectra of the reaction residues. Although this possibility has not been explored in the present work, the above observations could permit a successive development of one flask procedure for the selective reduction of ketonic groups in presence of aldehydic groups, in aprotic solvents.

Finally, we wish to report the results we obtained by treatment of methyl lithocholate **16** and methyl 3β-hydroxy-5α-etianate **18** with $(HAlN\text{-}i\text{-}Pr)_6$ in refluxing toluene.

Recently Kriz *et al.*[6] in a systematic investigation on the ability of this hydride to react with several functional groups reported that aliphatic esters were transformed in low yields in alcohols when the reaction was carried out in refluxing benzene. The principal compound, determined by gas-chromatography, was the corresponding amide.

As expected by the higher steric hindrance at C-20 than at C-24 of steroidal esters, reduction takes place in our case more readily with **16** than **18**, which was recovered in considerable amount (Table 2). It is noteworthy that unlike in the previous report[6] aldehydic compounds could be isolated from the reaction mixtures.

Table 2. Product distribution (%)

Ester	3-OH, CHO	Diol	Amide	Start. mat. recovered
16	30.5	16.5	21.5	4
18	13.0	15.5	26.5	36

Yields were calculated by NMR analysis of chromatographic fractions.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus and are uncorrected. Optical rotations were taken at 20° with a Schmidt–Haensch polarimeter in a 1 dm cell. IR spectra (KBr discs except for **8**) were recorded on a Perkin–Elmer 521 spectrophotometer. NMR spectra were measured with a Varian EM-390 spectrometer using, unless otherwise specified, deuteriochloroform as the solvent; chemical shifts are given in ppm (δ) from Me_4Si as internal standard. Mass spectra were obtained using a Hewlett–Packard 5980A spectrometer operating at an ionizing energy of 70 eV. Woelm basic alumina and silica Merck 60 (230–400 mesh) were used for column chromatography. Preparative layer chromatography (plc) was carried out with Merck HF_{254} silica gel (layers 0.5 mm thick). Light petroleum refers to 40–60°b.p. fraction. The drying agent was sodium sulphate. All the oxidations with chromium trioxide-pyridine complex and reductions with $(HAlN\text{-}i\text{-}Pr)_6$ were performed under a nitrogen atmosphere.

(20*S*)-22,23-*Dinor-5α-cholane-3β,24-diol* **15b**. Methyl (20*S*)-3β-acetoxy-22,23-dinor-5α-cholane-24-carboxylate[7] (5 g) was dissolved in dry THF (280 ml) and LAH_4 (2.8 g) was carefully added. After stirring at room temp for 1 hr the excess of the reagent was decomposed with the minimum amount of water, cooling at 0°. The THF soln was separated by filtration and the solid residue washed with the same solvent. The collected organic solns were passed through a column of basic alumina (Brockmann IV, 50 g), washing with THF. The resulting soln was evaporated under reduced pressure and the solid residue crystallised from MeOH to give **15b** (4.2 g), m.p. 231–232°; $[\alpha]_D$ +26° (*c*, 0.5 in CH_3CO_2H); ν_{max} 3260 (br), 1440, and 1035 cm^{-1}, δ (C_5D_5N) 0.67 (3H, s, 13-Me), 0.80 (3H, s, 10-Me), 3.51 and 3.84 (2H, A and B of ABX, J_{AB} = 13, J_{AX} = 6.5, J_{BX} = 3.5 Hz, C$\underline{H}_2$–OH). (Found: C, 78.18; H, 11.48. $C_{22}H_{38}O_2 \cdot 1/4\,H_2O$ requires: C, 77.93; H, 11.45%).

General procedure for the synthesis of steroidal ketoaldehydes. Following Ratcliffe and Rodehorst's procedure[4], CrO_3 (12 g, 120 mmol) was added to a vigorously stirred soln of 19 ml anhyd pyridine in 150 ml CH_2Cl_2. The deep burgandy soln was stirred for 15 min at room temp, then a soln of the diol (10mmol) in the minimum volume of dry THF was added dropwise. During this addition the temp was kept at 20–25°. After stirring an additional 30 min at room temp, the mixture was partitioned between sat Na_2CO_3 aq. and ether in excess. The organic layers were washed with 2N HCl, satd Na_2CO_3 aq., and water, dried and evaporated. The residue was purified on column chromatography (alumina Brockmann IV, 1:50) using benzene as eluent.

3-Oxo-5β-cholan-24-al **6**. Chromatographic purification of the residue (2.48 g) obtained from oxidation of **10**[8] (2.88 g), afforded pure **6** (2 g), m.p. 82–83° (from ether); $[\alpha]_D$ +39° (*c*, 1.0 in $CHCl_3$); ν_{max} 2735 (w) and 1718 cm^{-1}; δ 0.67 (3H, s, 13-Me), 1.00 (3H, s, 10-Me), 9.82 (1H, t, J = 2 Hz, CHO). (Found: C, 80.24; H, 10.67. $C_{24}H_{38}O_2$ requires: C, 80.39; H, 10.68%).

3-Oxo-5α-androstane-17β-carboxaldehyde **11a**. Elution of the residue (2.02 g) obtained from **15a**[9] (2.37 g) afforded pure **11a**[10] (1.9 g), m.p. 153–158°† (from ether); $[\alpha]_D$ +94° (*c*, 1.0 in $CHCl_3$); ν_{max} 2720 (w) and 1718 cm^{-1}; δ 0.75 (3H, s, 13-Me), 1.00 (3H, s, 10-Me), 9.81 (1H, d, J = 2 Hz, CHO). (Found: C, 79.40; H, 10.01. $C_{20}H_{30}O_2$ requires: C, 79.42; H, 10.00%).

(20S)-*3-Oxo-22,23-dinor-5α-cholan-24-al* **11b**. Usual treatment of the residue (1.23 g) arising from oxidation of **15b** (1.33 g), afforded pure **11b** (0.54 g), m.p. 152–153° (from ether–light petroleum); $[\alpha]_D$ +30° (*c*, 1.0 in $CHCl_3$); ν_{max} 2695 (w), 1720, and 1706 cm^{-1}; δ 0.72 (3H, s, 13-Me), 1.00 (3H, s, 10-Me), 9.60 (1H, d, J = 3.5 Hz, CHO). (Found: C, 79.72; H, 10.20. $C_{22}H_{34}O_2$ requires: C, 79.95; H, 10.37%).

Reduction of 3α,5-cyclo-5α-androstane-6,17-dione **1**. To a soln of **1**[11] (0.38 g) in 5 ml dry ether, was added 0.27 g of $(HAlN\text{-}i\text{-}Pr)_6$ in 10 ml dry ether. The mixture was refluxed for 3 hr and the excess of reagent was decomposed with the minimum amount of water, cooling at 0°. The soln was separated by filtration, washing the solid residue with EtOAc. The organic layers were collected, washed with water to neutrality, dried, and evaporated under reduced pressure to give a solid residue (0.4 g). Chromatography on silica (plc) [benzene–EtOAc (8:2) as eluent] yielded starting material (0.05 g), nearly pure **2** (0.21 g), m.p. 72–74° (from petrol–acetone); $[\alpha]_D$ +141° (*c*, 1.0 in $CHCl_3$) [lit.[3] m.p. 64–66° (from petrol–acetone), $[\alpha]_D$ + 133° (*c*, 1.0)]; ν_{max} 3510 and 1725 cm^{-1}; δ 0.25 (1H, apparent t, cyclopropyl), 0.87 (3H, s, 13-Me), 0.93 (3H, s, 10-Me), 3.96 (1H, dd, J = 4.5 and 11.5 Hz, 6β-H) (our NMR data agree with those previously reported[12]), and **3** (0.085 g), m.p. 178–180° (from ether); $[\alpha]_D$ +66° (*c*, 1.0 in CH_3OH) [lit[13] m.p. 176–177°, $[\alpha]_D$ +64.5° (dioxane)]‡; δ 0.19 (1H, apparent t, cyclopropyl), 0.73 (3H, s, 13-Me), 0.92 (3H, s, 10-Me), 3.6 (1H, m, 17α-H), 3.85 (1H, dd, J = 4.5 and 11.5 Hz, 6β-H).

Reduction of 3α,5-cyclo-5α-pregnane-6,20-dione **4**. To a solı of **4**[14] (0.535 g) in 5 ml dry benzene, was added 0.3 g poly(N isopropyliminoalane) in 10 ml dry ether. The mixture wa refluxed for 3 hr. After usual work the residue (0.58 g) wa chromatographed on silica (plc) [benzene–ether (9:1) a eluent], to give starting material (0.095 g) and **5** (0.365 g), m.p 151–152° (from ether); $[\alpha]_D$ + 157° (*c*, 1.0 in $CHCl_3$); ν_m 3550, 3010, and 1690 cm^{-1}; δ 0.24 (1H, apparent cyclopropyl), 0.62 (3H, s, 13-Me), 0.90 (3H, s, 10-Me), 3.9 (1H, dd, J = 4.5 and 11.5 Hz, 6β-H). (Found: C, 79.59; H 10.24. $C_{21}H_{32}O_2$ requires: C, 79.70; H, 10.19%).

General procedure for reduction by poly(N isopropyliminoalane) of steroidal ketoaldehydes. To one mm ketoaldehyde in 5 ml dry benzene, was added 0.34 mm $(HAlN\text{-}i\text{-}Pr)_6$ in 5 ml dry benzene. The mixture was stirred f 1 hr at room temp. After conventional work up, the combine organic soln (the inorganic solid was washed with EtOA gave a residue which was chromatographed on silica (pl [benzene–EtOAc (8:2) as eluent].

Reduction of 3-oxo-5β-cholan-24-al **6**. Chromatography the residue (0.58 g) obtained by reduction of **6** (0.54 afforded (a) starting material (0.05 g), (b) **8** (0.03 g) as an o $[\alpha]_D$ +24° (*c*, 1.0 in $CHCl_3$); ν_{max} ($CHCl_3$) 3600, 2715, a

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† Sample inserted into a Büchi oil bath at 140°; m.p. 190–196° on a Kofler hot-stage apparatus.

‡ Wagner *et al.*[13] indicated this compound as the epimeric 6β,17β-diol.

1720 cm^{-1}; δ 0.64 (3H, s, 13-Me), 0.94 (3H, s, 10-Me), 4.11 (1H, m, 3α-H), 9.81 (1H, t, J = 2 Hz, CHO). (Found: C, 77.93; H, 11.06. $C_{24}H_{40}O_2 \cdot 1/2\,H_2O$ requires: C, 77.99; H, 11.18%); (c) **7** (0.105 g) identical with a sample obtained from reduction with $(HAlN\text{-}i\text{-}Pr)_6$ of **16**; (d) **9** (0.065 g), m.p. 112–113° (from ether–light petroleum); $[\alpha]_D$ +36° (*c*, 1.0 in $CHCl_3$) [lit.[15] 115.5 116.5°; $[\alpha]_D$ +34.1 ± 2° (c 0.946 in $CHCl_3$); (e) 5β-cholane-3β,24-diol (0.04 g), m.p. 151–152° (from EtOAc) [lit.[16] m.p. 150–151.5° (from MeOH)]; $[\alpha]_D$ +23° (*c*, 1.0 in $CHCl_3$) [lit.[17] $[\alpha]_D$ +24.2° (*c*, 1.9 in $CHCl_3$)]; and (f) **10** (0.11 g) identical with an autentical sample.[8]

Reduction of 3-oxo-5α-androstane-17β-carboxaldehyde **11a**. Usual chromatography of the residue (0.69 g) obtained from **11a** (0.66 g), yielded (a) starting material (0.065 g); (b) **13a** (0.035 g), m.p. 137–138° (from ether–light petroleum); $[\alpha]_D$ + 56° (*c*, 1.0 in $CHCl_3$); ν_{max} 3400–3300 (broad), 2715 (w), and 1715 cm^{-1}; δ 0.74 (3H, s, 13-Me), 0.79 (3H, s, 10-Me), 4.05 (1H, m, 3β-H), 9.81 (1H, d, J = 2 Hz, CHO); mass spectrum *m/e* 304 (M^+). (Found: C, 78.36; H, 10.63. $C_{20}H_{32}O_2$ requires: C, 78.89; H, 10.59%); (c) **12a** (0.105 g) identical with a sample obtained by reduction with $(HAlN\text{-}i\text{-}Pr)_6$ *of* **18**; (d) **14a** (0.145 g), m.p. 158–160° (from ether); $[\alpha]_D$ + 33° (*c*, 1.0 in $CHCl_3$) [lit.[10] m.p. 158-161°; $[\alpha]_D$ +33.4°] and finally (e) a mixture of diols (0.18 g) detected by NMR.

Reduction of (20S)-*3-oxo-22,23-dinor-5α-cholan-24-al* **11b**. The residue (0.65 g) obtained from reduction of **11b** (0.6 g) gave after usual separation,† (a) starting material (0.065 g); (b) **13b** (0.03 g), m.p. 160–162° (from ether); $[\alpha]_D$ + 18° (*c*, 1.0 in $CHCl_3$); ν_{max} 3280, 2710 (w), and 1725 cm^{-1}; δ 0.70 (3H, s, 13-Me), 0.79 (3H, s, 10-Me), 4.05 (1H, m, 3β-H), 9.61 (1H, d, J = 3.5 Hz, CHO); mass spectrum *m/e* 332 (M^+); (c) a mixture (0.23 g) of **12b** and **14b** (48% of **12b** and 52% of **14b** relative yields determined by NMR analysis), which was resolved by silica (plc) [CH_2Cl_2–light petroleum (3:1) as eluent] to give pure **12b**, m.p. 158–160° (from ether–light petroleum); $[\alpha]_D$ + 11° (*c*, 1.0 in $CHCl_3$), ν_{max} 3400 (broad), 2710 (w), and 1725 cm^{-1}; δ 0.70 (3H, s, 13-Me), 0.81 (3H, s, 10-Me), 3.59 (1H, m, 3α-H), 9.59 (1H, d, J = 3.5 Hz, CHO); mass spectrum *m/e* 333 (M^+), and **14b**, m.p. 173° (from ether); $[\alpha]_D$ + 37° (*c*, 1.0 in $CHCl_3$), ν_{max} 3450 and 1700 cm^{-1}; δ 0.70 (3H, s, 13-Me), 1.00 (3H, s, 10-Me), 3.50 (2H, AB part of an ABX system, J_{AB} = 11, J_{AX} = 6.5, J_{BX} = 3.5 Hz, $C\underline{H}_2OH$); mass spectrum *m/e* 333 (M^+), and finally (d) a mixture (0.185 g) of diols detected by NMR.

Reduction of methyl lithocholate **16**. To **16**[18,19] (0.59 g) in 6 ml dry toluene, was added 0.325 g $(HAlN\text{-}i\text{-}Pr)_6$ in 6 ml dry toluene. The mixture was refluxed for 3 hr. Conventional work up gave a residue which was chromatographed on silica (plc) [benzene–ethyl acetate (7:3) as eluent] to afford (a) nearly pure starting material (0.025 g), (b) **7** (0.165 g), m.p. 145–146° (from ether–light petroleum); $[\alpha]_D$ + 29° (*c*, 1.0 in $CHCl_3$) (lit.[20] m.p. 146-149°, $[\alpha]_D$ +28°); (c) **10** (0.1 g) and (d) **17** (0.135 g), m.p. 227–228° (from CH_3OH–ether); $[\alpha]_D$ + 36° (*c*, 0.5 in $CHCl_3$); ν_{max} 3445, 3325 and 1650 cm^{-1}, δ 0.65 (3H, s, 13-Me), 0.91 (3H, s, 10-Me), 1.13 [6H, d, J = 6.5 Hz, $CH(C\underline{H}_3)_2$], 3.63 (1H, m, 3β-H), 4.09 [1H, m, $C\underline{H}(CH_3)_2$]. (Found: C, 77.56; H, 11.42; N, 3.26. $C_{27}H_{47}NO_2$ requires: C, 77.64; H, 11.34; N, 3.35%).

Reduction of methyl 3β-hydroxy-5α-etianate **18**. To **18**[21] (0.98 g) in 10 ml dry toluene, was added 0.62 g $(HAlN\text{-}i\text{-}Pr)_6$ in 12 ml dry toluene and the mixture was refluxed for 3 hr. After usual work up the residue was chromatographed on a column of silica (1:30). Elution with benzene–EtOAc (8:2) gave a mixture (0.48 g) of starting material **18** and aldehyde **12a** (73% of **18** and 27% of **12a** relative yields inferred by NMR analysis). Alkaline hydrolysis of **18** allowed to isolate **12a**, m.p. 168–170° (from ether–light petroleum); $[\alpha]_D$, NMR, and IR data in accord with those previously reported.[22-24]. Elution with benzene–EtOAc (1:1) afforded **15a** (0.135 g), identical with an autentical sample,[9] and **19** (0.28 g), m.p. 201-202° (from MeOH), $[\alpha]_D$ +41° (*c*, 0.5 in CH_3OH); ν_{max} 3300–3250 and 1640 cm^{-1}; mass spectrum *m/e* 362 (M^+), identical with a sample obtained following the procedure of Evans.[25]

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REFERENCES

[1] M. Paglialunga Paradisi, G. Pagani Zecchini and A. Romeo, *Tetrahedron Letters* 2369 (1977).

[2] J. Tadanier and W. Cole, *J. Org. Chem.* **27**, 4610 (1962).

[3] G. D. Meakins, personal communication and Ref. 12.

[4] R. Ratcliffe and R. Rodehorst, *J. Org. Chem.* **35**, 4000 (1970).

[5] H. C. Brown and Surendra U. Kulkarni, *Ibid.* **42**, 4169 (1977).

[6] O. Kriz, J. Stuchlik and B. Casensky, *Z. Chem.* **17**, 18 (1977).

[7] E. Fernholz, *Ann. Chim.* **507**, 128 (1933).

[8] L. F. Fieser, J. E. Herz, M. W. Klohs, M. A. Romero and T. Utne, *J. Am. Chem. Soc.* **74**, 3309 (1952).

[9] F. Sallmann and C. Tamm, *Helv. Chim. Acta* **39**, 1340 (1956).

[10] J. Wicha and A. Zarecki, *Tetrahedron Letters* 3059 (1974).

[11] A. Butenandt and L. A. Suranyi, *Ber. Dtsch. Chem. Ges.* **75B**, 591 (1942).

[12] V. E. M. Chambers, W. A. Denny, E. R. H. Jones, G. D. Meakins, J. O. Miners, J. T. Pinhey and A. L. Wilkins, *J. Chem. Soc.* Perkin I, 1359 (1975).

[13] A. F. Wagner, N. E. Wolff and E. S. Wallis, *J. Org. Chem.* **17**, 529 (1952).

[14] F. Khuong-Huu, D. Herlem and J. J. H. Simes, *Bull. Soc. Chim. Fr.* 258 (1969).

[15] S. Hayakawa, Y. Kanematsu and T. Fujiwara, *Biochem. J.* **115**, 249 (1969).

[16] R. T. Blickenstaff and F. C. Chang, *J. Am. Chem. Soc.* **80**, 2726 (1958).

[17] H. R. Nace and E. Manners Holt, *J. Org. Chem.* **34**, 2692 (1969).

[18] C. H. Issidorides, M. Fieser and L. F. Fieser, *J. Am. Chem. Soc.* **82**, 2002 (1960).

[19] F. C. Chang, R. T. Blickenstaff, A. Feldstein, J. Ransom Gray, G. S. McCaleb and D. H. Sprunt, *Ibid.* **79**, 2164 (1957).

[20] A. V. McIntosh, A. M. Searcy, E. M. Meinzer and R. H. Levin, *Ibid.* **71**, 3317 (1949).

[21] M. Steiger and T. Reichstein, *Helv. Chim. Acta* **20**, 1040 (1937).

[22] Roussel-Uclaf, Belgian Patent 635,878 (1964); *Chem. Abstr.* **62**, 14781f (1965).

[23] A. Gelbart and R. Thomas, *J. Med. Chem.* **21**, 284 (1978).

[24] H. Hikino, T. Okuyama, S. Arihara, Y. Hikino, T. Takemoto, H. Mori and K. Shibata, *Chem. Pharm. Bull.* **23**, 1458 (1975).

[25] D. A. Evans, *Tetrahedron Letters* 1573 (1969).

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† NMR analysis of chromatographic functions seems to indicate limited isomerization at C-20 center of the aldehydic compounds. Physical and spectral data refer to (20s) epimers.