ether (10 ml) at 0°, anhydrous aluminum chloride (10 mg) was added, followed by excess ethereal diazomethane, until the yellow color persisted briefly. Further aluminum chloride and diazomethane solution were then added. After 30 min of stirring at 0°, glacial acetic acid was added dropwise to destroy excess diazomethane. Work-up as in the methylation of **9** described above gave a material shown by tlc to comprise the methoxy lactone **7** and a small amount of the hydroxy lactone **12**. No methoxy lactone **8** was observed.

Reductions of Lactone 7 and 8 with Lithium Aluminum Hydride.—The lactone **7** (50 mg) was heated under reflux in dioxane (5 ml) with lithium aluminum hydride (10 mg) for 4 hr. The reaction was quenched with aqueous dioxane and worked up *via* 2 *N* HCl and ether. The product was the methoxy diol **11** (20 mg), which crystallized from ethyl acetate–hexane as needles: mp 190.5–191.5°; $[\alpha]^{23}D$ −60° (*c* 1.0, $CHCl_3$); ν^{KBr} 3400 cm^{-1} (OH). *Anal.* Calcd for $C_{33}H_{54}O_3$: C, 79.46; H, 10.92. Found: C, 79.32; H, 10.90.

Lactone **8**, reduced in the same way, gave the same methoxydiol.

Reductions of the Methoxy Anhydride 6 with Lithium Aluminum Hydride and Sodium Aluminum Hydride. 1. With Lithium Aluminum Hydride.—A solution of the methoxy anhydride **6** (500 mg) in tetrahydrofuran (5 ml) was added dropwise to a stirred solution of lithium aluminum hydride (40 mg) in tetrahydrofuran (5 ml) at −55° (acetone–CO_2 bath). The mixture was let warm to −5° during 90 min and stirred at this temperature for 30 min, after which it was acidified (6 *N* HCl) and partitioned between water and ether. The organic material obtained by concentration of the dried (Na_2SO_4) ether layer was chromatographed as described for the reduction of **6** with sodium borohydride above. Lactones **7** and **8** were obtained pure in yields of 200 and 15 mg, respectively. They were identified by tlc and ir.

2. With Sodium Aluminum Hydride.—From 525 mg of anhydride **6** and 100 mg of sodium aluminum hydride (Ventron), lactone **7** and **8** were obtained in yields of 275 and 30 mg, respectively, using the same procedure as above.

Reduction of the Methoxy Anhydride 6 with Lithium Aluminum Tri-*tert*-butoxyhydride.—A solution of the anhydride **6** (1 g) in tetrahydrofuran (25 ml) was added dropwise to a stirred solution of lithium aluminum tri-*tert*-butoxyhydride (2.0 g) in tetrahydrofuran (25 ml) at 0°. After 5 hr at 0°, the reaction was quenched with excess 2 *N* HCl, and the mixture partitioned between water and ether. The ether layer was dried ($MgSO_4$) and concentrated, and the organic product chromatographed on preparative silica gel plates as in experiments described above, except that pentane–ethyl acetate (10:1) was used as developing solvent. After four developments, three bands were discerned: one at the origin and two above it. Extraction of the lower two of these as above gave the same material which was the lactol **13**, obtained from ether as fine needles (650 mg): mp 234–237° dec; $[\alpha]^{23}D$ −51° (*c* 1.0, $CHCl_3$); ir ν^{KBr} 3404, 3230 (OH), 1770 (γ-lactone), 1735 cm^{-1} (aldehyde and acid C=O); ν^{CHCl_3} 3300 (OH), 1765 cm^{-1} (γ-lactone). *Anal.* Calcd for $C_{33}H_{50}O_4$: C, 77.60; H, 9.87. Found: C, 77.68; H, 9.69. Treatment of this compound (50 mg) with acetic anhydride (2 ml) under reflux (N_2) for 3 hr and removal of solvent under reduced pressure gave a slowly crystallizing oil, which after two recrystallizations from ethyl acetate–hexane gave the pure lactol acetate **15** as needles: mp 170–172°; ir ν^{KBr} 1780 (γ-lactone C=O), 1755 cm^{-1} (lactol acetate C=O); nmr τ 3.69, 4.12 (2 H, AB quartet, J = 10 Hz, C-6, C-7 H), 3.87 (1 H, broadened singlet, C-3′ H), 4.82 (2 H, m, C-22, CH23 H), 6.63 (3 H, singlet, C-3 OCH_3), 7.85 (3 H, singlet, lactol CH_3COO), 8.91 (3 H, singlet, C-19 CH_3), 9.24 (3 H, singlet, C-18 CH_3). *Anal.* Calcd for $C_{35}H_{52}O_5$: C, 76.04; H, 9.48. Found: C, 76.13; H, 9.50. The highest band in the preparative tlc from the reduction was present in very small amount. Analytical tlc of this band showed it to contain two compounds, one identical with the methoxy lactone **7**. Reduction of a very small sample of this mixture with sodium borohydride in ethanol and work-up as above gave (tlc) a mixture containing methoxy lactone **7** and **8** only.

Similar sodium borohydride reduction of the pure lactol **13** gave the methoxy lactone **7**.

Registry No.—**1**, 30345-18-7; **2**, 30345-11-0; **6**, 30345-12-1; **7**, 30345-13-2; **8**, 30409-20-2; **10**, 30345-14-3; **11**, 30345-15-4; **13**, 30345-16-5; **15**, 30345-17-6.

Acknowledgments.—We thank Mr. Yoichi Shimokawa for assistance with ORD–CD measurements, and we gratefully acknowledge partial support of this work through institutional research grants from the American Cancer Society to The University of Michigan.

Steroids. VIII.[1] A-Nor Steroids *via* Pinacol-Type Rearrangement

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Received December 23, 1970

Pinacol-type rearrangement of 2α-hydroxy-3α-mesyloxy-2β-methylcholestane led to 2β-acetyl-1-norcholestane, the structure and stereochemistry of which was confirmed by Baeyer–Villiger oxidation to the known 2β-acetoxy-*A*-norcholestane and subsequent saponification and oxidation to the known *A*-norcholestan-2-one. Analogous rearrangement of 3β-hydroxy-4β-mesyloxy-3α-methyl-5β-cholestane gave 3ξ-acetyl-*A*-nor-5β-cholestane.

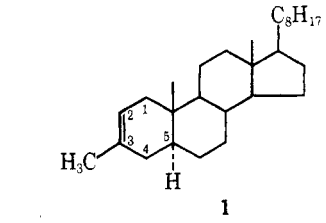
In the course of a synthesis of steroids with modified ring systems,[2] it was necessary to contract the A ring of certain steroids and introduce the progesterone side chain. The synthesis of A-nor steroids has been effected previously through the Favorskii reaction or the benzilic acid rearrangement.[3–7] Since these methods were not particularly suited to our objectives, a pinacol-type rearrangement was studied. This approach has been used for the modification of the D ring of steroids.[8,9] After the completion of our work, the preparation of A-homo-B-nor and A-nor-B-homo steroids[10] and ring-contracted pinane derivatives[11] through a pinacol-type rearrangement was described.

Reaction of 3-cholestanone with methylmagnesium bromide gave a tertiary alcohol which could be dehydrated readily[12] to an olefin **1**. The nmr spectrum of **1**

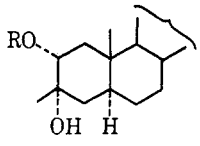
(1) For part VII, see A. K. Bose and N. G. Steinberg, *Syn.*, 595 (1970).
(2) N. G. Steinberg, Ph.D. Thesis, Stevens Institute of Technology, 1969.
(3) F. Winternitz and A. C. dePaulet, *Bull. Soc. Chim. Fr.*, 288 (1954).
(4) D. E. Evans, A. C. dePaulet, C. W. Shoppee, and F. Winternitz, *Chem. Ind. (London)*, 355 (1955).
(5) D. E. Evans, A. C. dePaulet, C. W. Shoppee, and F. Winternitz, *J. Chem. Soc.*, 1451 (1957).
(6) J. Bielman and N. Rajic, *Bull. Soc. Chim. Fr.*, 441 (1962).
(7) For an excellent summary, see N. L. Wendler in "Molecular Rearrangements," Vol. 2, P. de Mayo, Ed., Interscience, New York, N. Y., 1964, p 1084.
(8) N. L. Wendler and D. Taub, *J. Amer. Chem. Soc.*, **82**, 2836 (1960).
(9) G. Stork and J. E. McMurry, *ibid.*, **89**, 5465 (1967).
(10) M. Nussim and Y. Mazur, *Tetrahedron*, **24**, 5337 (1968).
(11) R. G. Carlson and J. K. Pierce, *Tetrahedron Lett.*, 6213 (1968).
(12) D. H. R. Barton, A. da S. Campos-Neves, and R. C. Cookson, *J. Chem. Soc.*, 3500 (1956).

was consistent with the 3-methyl-2-cholestene structure, since the olefinic proton signal appeared as a multiplet rather than a doublet. The corresponding olefin **8** from 3-coprostanone could be assigned the 3-methyl-5β-cholest-3-ene structure as the olefin signal was a doublet (J = 2 Hz).

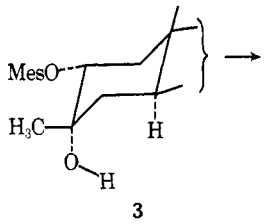
The pinacol-type rearrangement of 3-methyl-2,3-diol (**2**) could lead to various products depending on the configurational and conformational factors.[13] Besides the desired 2-acetyl-*A*-norcholestane (**4**), other products could be 2,3-epoxide and 2-methyl-3-cholestanone. It is known[14] that the optimum conditions for ionic rearrangement in substituted cyclohexanes exist when the four atoms involved in the rearrangement are coplanar and the migrating and departing groups are trans and antiparallel. In the light of these requirements, the best chances for obtaining **4** would exist when the 2,3-diol is cis and α oriented.



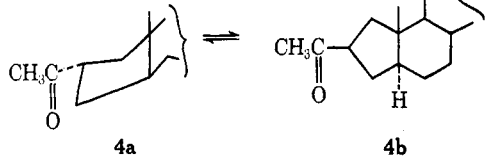
1



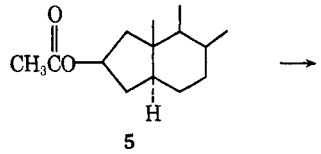
2, R = H
3, R = Mes



3



4a **4b**



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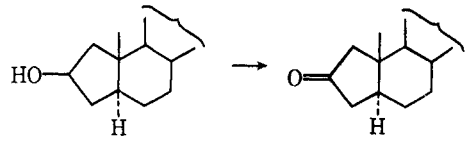
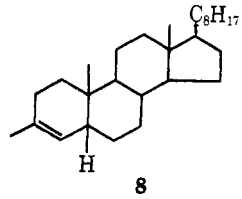


6 **7**

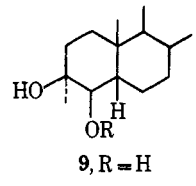
Stereospecific formation of a diol **2** occurred on osmylation of **1**. Confirmation of the expected 2α,3α configuration for the diol was provided by its nmr spectrum: the 2β proton appeared as a quartet (J_{aa} = 12 Hz, J_{ae} = 6 Hz). The 2α-mesylate derivative **3** underwent ring contraction to give a single isomer of 2-acetyl-*A*-norcholestane (**4**) in 73% yield when warmed with a solution of 5% methanolic potassium hydroxide. The 2α configuration would be expected for the acetyl group in **4** on the basis of the reaction mechanism; however, epimerization in the presence of a base could result in the formation of the β isomer **4b**.

Shoppee and Sly[15] had prepared 2α- and 2β-acetyl-*A*-nor-5α-cholestane but the configurational assignment was later reversed by Fuchs and Loewenthal,[16] a revision subsequently confirmed by Dauben, *et al.*[17] Baeyer–Villiger oxidation of **4** gave the previously described 2β-acetoxy-*A*-nor-5α-cholestane in good yield which was hydrolyzed and oxidized to the known *A*-norcholestan-2-one. The product isolated by us from the ring contraction of **3** must therefore be assigned the structure **4b**.

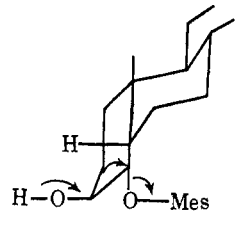
It could be expected by analogy that ring contraction of an appropriate 5β-steroid compound by the sequence described above would lead to an A-nor derivative with an acetyl side chain on C-3 (**11**). Reaction of 3-coprostanone with methylmagnesium iodide followed by dehydration gave a single cycloalkene **8**, demonstrating regiospecificity of the dehydration step. Osmylation



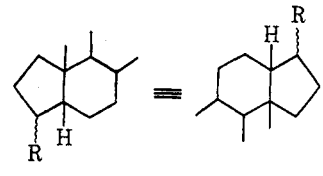
8



9, R = H



10



11, R = CH_3CO
12, R = CH_3CO_2

of **8** afforded in good yield a cis diol **9**, the stereochemistry of which was determined by nmr spectroscopy. The methine proton at C-4 exhibited a doublet at τ 6.38 with a coupling constant of 11 Hz indicative of diaxial coupling with the 5β proton. The compound **9** must therefore be the 3β,4β diol. Conversion of **9** to the mesylate **10** followed by alkali treatment yielded 3ξ-acetyl-5β-cholestane (**11**). Baeyer–Villiger oxidation of **11** gave 3-acetoxy-5β-cholestane (**12**) as an oil which appeared to be homogenous on tlc. Although the initial product from the ring contraction of **10** would be expected to be the 3β-acetyl compound on mechanistic grounds, inversion (at least in part) may have occurred under the basic reaction conditions.

Since bile acids belong to the 5β series and are readily available, the pinacol-type rearrangement described here provides easy access to 18-nor-14β-methylprogesterone derivatives **11**. Work along these lines is in progress.

Experimental Section

Infrared spectra were obtained in Nujol mull on a Perkin-Elmer Model 137B spectrophotometer; nmr spectra were re-

(13) For example, see ref 11.
(14) D. H. R. Barton, *J. Chem. Soc.*, 1027 (1953).
(15) C. W. Shoppee and J. C. P. Sly, *ibid.*, 345 (1959).
(16) B. Fuchs and H. J. E. Loewenthal, *Tetrahedron*, **11**, 199 (1960).
(17) W. G. Dauben, G. A. Boswell, and W. H. Templeton, *J. Amer. Chem. Soc.*, **83**, 5006 (1961).

corded in deuteriochloroform solution on a Varian DP-60 spectrometer using tetramethylsilane as an internal standard. Melting points were determined on Mel-Temp block and are uncorrected. Thin layer chromatography was performed on silica gel G coated plates and spots were visualized with iodine vapor.

3-Methylcholest-2-ene (1).—To a stirred solution of 6.06 g (15.8 mmol) of cholestan-3-one in 21 ml of anhydrous tetrahydrofuran was added 21 ml of 3 *N* methylmagnesium bromide. After refluxing the mixture in a nitrogen atmosphere for 1 hr and then cooling, the excess of Grignard reagent was decomposed by dropwise addition of saturated ammonium chloride solution. The layers were separated, and the aqueous layer was extracted three times with chloroform. The organic extracts were combined, washed successively with saturated aqueous sodium chloride and water, and dried (Na_2SO_4). Evaporation *in vacuo* gave 5.8 g (91%) of the *tert*-alcohol (ir, 2.8 μ) as an oil, which could not be induced to crystallize.

A solution of 4.0 g (9.95 mmol) of this alcohol in 60 ml of glacial acetic acid was heated at reflux for 10 hr. After cooling, a crude solid precipitated which was collected and washed with a small amount of acetic acid and water and then chromatographed over neutral alumina. Elution with chloroform afforded 3.5 g (92%) of a colorless solid, mp 82–83° (lit.[12] mp 82–83°). The nmr spectrum displayed a one-proton multiplet at τ 4.8 (olefin).

3β-Methylcholestane-2α,3α-diol. (2).—A solution of 2.28 g of 1 in 20 ml of dioxane was treated with a solution of 2.28 g of osmium tetroxide in 5 ml of benzene. The solution was stirred at room temperature for 2 days, treated with 92 ml of absolute alcohol for 45 min, and then reduced with a solution of sodium sulfite at 5° for 3 hr. The reaction mixture was filtered through Super-cel, and the cake thoroughly washed with absolute alcohol and then with ether.

The filtrates were combined and evaporated to dryness *in vacuo*. The crude product was once again taken up in ether, washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The residue, on crystallization from ethyl acetate, afforded 1.5 g (61%) of 2, mp 162–164°. An analytical sample, mp 188–189°, was obtained by chromatography over neutral alumina and recrystallization from ethyl acetate–acetone. The nmr spectrum revealed a one-proton quartet at τ 6.5, J = 12 Hz (5a,a) and J = 6 Hz (5a,e).

Anal. Calcd for $C_{28}H_{50}O_2$: C, 80.01; H, 11.61. Found: C, 80.09; H, 11.51.

2β-Acetyl-*A*-nor-5α-cholestane (4).—To a stirred solution of 1.0 g (2.4 mmol) of 2 dissolved in 10 ml of pyridine was added 1.5 ml of methanesulfonyl chloride at −5–0°. After 2 hr at that temperature, the reaction mixture was poured into water and allowed to stand for 30 min. The resulting precipitate was dissolved in chloroform, washed three times with water, and dried (Na_2SO_4). Removal of solvent afforded 1.2 g (100%) of 3 which was used without purification for the next step.

A mixture of 1.2 g of crude 3 in 40 ml of methanol and 1.8 g of potassium hydroxide in 4 ml of distilled water was refluxed for 1 hr, under nitrogen. The reaction mixture was cooled to 0–5°, acidified to pH 1 with 2.5 *N* aqueous HCl, and extracted with three portions of chloroform. The usual work-up gave 0.98 g of a crude product which was chromatographed over neutral alumina to afford 0.68 g (71%) of 4, mp 56–57.5°, characterized by infrared absorption at 5.78 μ (CO) and a methyl signal [$CH_3C(=O)$] at τ 7.98 in the nmr spectrum. An analytical sample, mp 62–64°, was prepared by recrystallization from methanol.

Anal. Calcd for $C_{28}H_{48}O$: C, 83.93; H, 12.08. Found: C, 83.60; H, 12.32.

2β-Acetoxy-*A*-nor-5α-cholestane (5).—A solution of 100 mg of 4 and 188 mg of *m*-chloroperbenzoic acid in 5 ml of chloroform was maintained at 0–5° for 7 days and then treated with 5% aqueous potassium iodide, followed by 5% aqueous solution of sodium thiosulfate. After three washes with water, the organic layer was dried ($MgSO_4$) and evaporated to give a material with strong ir absorption at 5.78 μ (ester CO) which upon crystallization from methanol afforded 80 mg (77%) of 5, mp 75–76° (lit.[17] 75–77°).

***A*-nor-5α-cholestan-2-one** (7).—A solution of 100 mg of 5 in methanol and 2 ml of a 10% solution of potassium hyroxide was refluxed under nitrogen for 1 hr. After the usual work-up 95 mg of product 6 was obtained which was dissolved in acetone and oxidized with Jones reagent at 0–5°. Methanol was added to destroy the excess of Jones reagent. The reaction mixture was diluted with water and then extracted with ether. The combined organic extracts were washed with water, 10% aqueous sodium bicarbonate, and again with water. Drying ($MgSO_4$) and concentration *in vacuo* afforded 90 mg of an oil which was chromatographed on 6.0 g of silica gel to yield 35 mg of the title compound, mp 95–96°. The infrared spectrum showed an absorption peak at 5.75 μ; in the mass spectrum the molecular ion appeared at *m/e* 372 (M calculated for $C_{26}H_{44}O$). The 2,4-dinitrophenylhydrazone had mp 166–167.5° (lit.[15] mp 165–167°).

3-Methyl-5β-cholest-3-ene (8).—Following the method for the preparation of 1, coprostanone was converted to 5 in about 90% yield and isolated as an oil characterized by the presence of a methyl signal as a doublet (J = 2 Hz) at τ 8.32 in the nmr spectrum.

Anal. Calcd for $C_{28}H_{48}$: C, 87.42; H, 12.54. Found: C, 87.48; H, 12.60.

3α-Methylcoprostane-3β,4β-diol (9).—A solution of 730.3 mg (1.9 mmol) of 5 in 10 ml of dioxane was treated with a solution of 1.5 g of osmium tetroxide in 8 ml of benzene. After 2 days at room temperature, the reaction mixture was thoroughly washed with absolute alcohol (20 ml) and then treated with a solution of sodium sulfite at 5° for 3 hr. The reaction mixture was filtered through Super-cel, and the cake was washed with absolute alcohol and then ether. The organic combined filtrate and washes were evaporated to dryness *in vacuo*. The resulting crude product was dissolved in ether, washed with water, dried (Na_2SO_4), and evaporated to give 391.8 mg of oil. This oil was dissolved in chloroform, adsorbed on 12 g of neutral alumina, and eluted successively with chloroform and then chloroform–methanol (99:1), from which 262 mg (33%) of oil was obtained which gave a single spot on tlc: nmr τ 5.38 (J_{aa} = 11 Hz); mass spectrum molecular ion at *m/e* 418 (M calculated for $C_{28}H_{50}O_2$).

3β-Mesyl-3α-methylcoprostan-3β-ol (10).—A solution of 216.8 mg (0.63 mmol) of 9 was dissolved in 2.5 ml of pyridine and treated with 0.6 ml of methanesulfonyl chloride at 0–5°, with constant stirring. The reaction mixture was allowed to stand for 3 hr at 0–5° and poured into water. After 30 min, the resulting oil was dissolved in chloroform, washed three times with water, dried (Na_2SO_4), and evaporated to give 247 mg of an oil. The infrared spectrum of the mesylated product showed mesylate absorption at 7.5 (s) and 8.5 μ, as well as hydroxyl absorption at 2.85 μ. This product was satisfactory for use in the next step.

3ξ-Acetyl-*A*-nor-5β-cholestane (11).—A solution of 240 mg (0.49 mmol) of 10 in 1 ml of methanol was treated with a solution of 230 mg of potassium hydroxide in 0.5 ml of water and refluxed for 1 hr, under an inert atmosphere. The reaction was cooled to 0–5°, acidified to pH 1 with 2.5 *N* aqueous hydrochloric acid, and extracted three times with ether. The ethereal solution was washed with water, dried (Na_2SO_4), and evaporated to give 188 mg of product 11 which was dissolved in hexane, adsorbed on 6.0 g of neutral alumina, and eluted successively with hexane, and hexane–benzene (1:1). The latter eluent mixture afforded 148 mg (75.5%) of an oily product which was homogeneous by tlc. The infrared spectrum showed absorption peaks at 5.85 μ; nmr τ 7.87 (s, 3 H, [$CH_3C(=O)$]; mass spectrum molecular ion *m/e* 400 (M calculated for $C_{28}H_{48}O$).

Registry No.—2, 20297-26-1; **4b**, 2493-91-6; **5**, 14772-59-9; **7**, 2310-36-3; **8**, 30255-99-3; **9**, 30256-00-9; **10**, 30256-01-0; **11**, 30256-02-1.