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Synthesis of Bridged Steroids. III.[1] Cholestane Derivatives having a Bridged Bicyclo[2.2.2]octane Ring System of the Atisine Type

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Synthesis of the cholestane derivative (V) having a bridged bicyclo[2.2.2]octane ring system of the atisine type was attained by various routes starting from 5α-cyanocholestan-3-one (II) as illustrated in Chart 4. The route through the ketal aldehyde (X) and 5α-vinylcholestan-3-one 3-ethylene ketal (XV), the key intermediate for the present synthesis, was found to be most advantageous. However, another route through the bridged acetoxy mesylate (XVI) is also thought to be important, since this intermediate is commonly used for the synthesis of the kaurene-type bridged ring compounds as described in the preceding paper.[1] The allylic alcohol function of the atisine type was introduced at the corresponding position with opposite configuration of the hydroxy group giving compound (XXXVIII).

In the preceding paper,[1] we reported synthesis of cholestane derivatives having a bicyclo-[3.2.1]octane ring system of the kaurene type. In the present paper, we describe synthesis of related cholestane derivatives having a bridged bicyclo[2.2.2]octane ring of the atisine type. This work was carried out in the hope of finding some biologically interesting compounds and also to establish a possible route for synthesis of atisine (I),[3] a diterpene alkaloid.

For this purpose, we started from 5α-cyanocholestan-3-one (II), since the angular cyano group of this compound provides a suitable basement for construction of any of the bridged

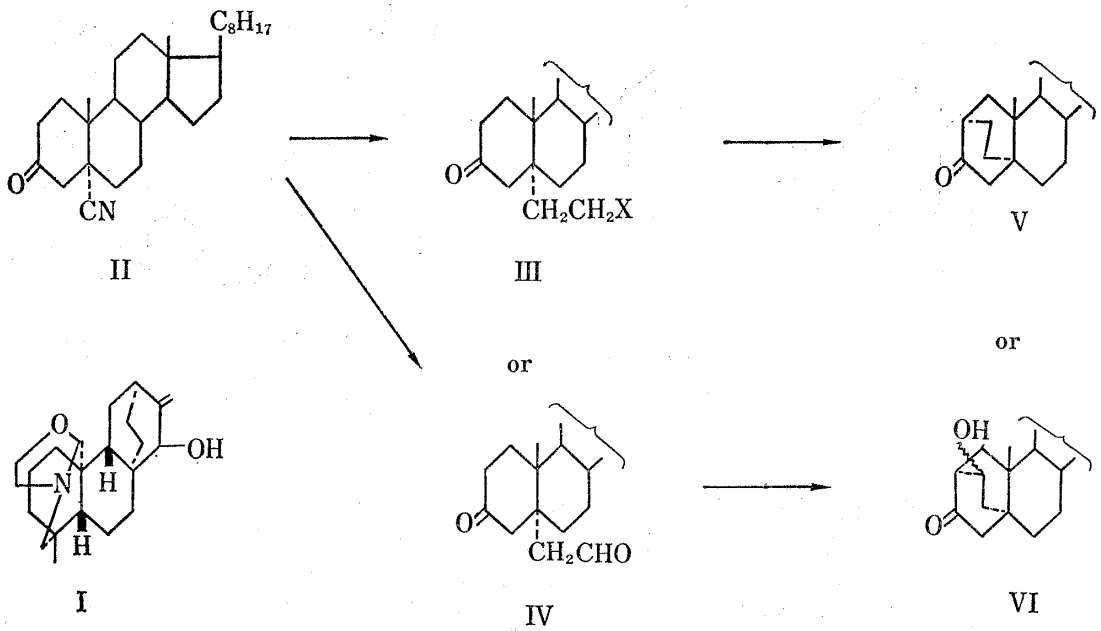

Chart 1

1) Part II: W. Nagata, M. Narisada, and T. Wakabayashi, *Chem. Pharm. Bull.* (Tokyo), **16**, 875 (1968).
2) Location: *Fukushima-ku, Osaka.*
3) W. Nagata, T. Sugasawa, M. Narisada, T. Wakabayashi, and Y. Hayase, *J. Am. Chem. Soc.*, **85**, 2342 (1963); *ibid.*, **89**, 1483 (1967).

rings as recognized from the foregoing papers.[1,4] The work comprises lengthening of the cyano group to a two-carbon chain having an appropriate functional group at the terminal position as shown in III (X represents an appropriate leaving group) or IV, followed by cyclization giving compound (V) or (VI) with objective bridged ring.

For obtaining the homoacid ester (XIIa) the Arndt-Eistert reaction was first applied to the keto carboxylic acid (VII) prepared from the cyano ketone (II) through several steps.[5] The keto acid (VII) is known to exist exclusively in the bridged form (VIIa) in the crystalline state and preponderant in a chloroform solution. Therefore, the usual method using thionyl chloride will not be employed to convert VIIa into the acid chloride (VIII). However, the sodium salt of this acid was found to exist in the open form (VII) as judged by the absence of the γ-lactone band in the Nujol infrared. The salt was, therefore, treated with oxalyl chloride[6] giving a chlorine-containing oily product. Unfortunately, the product was composed mainly

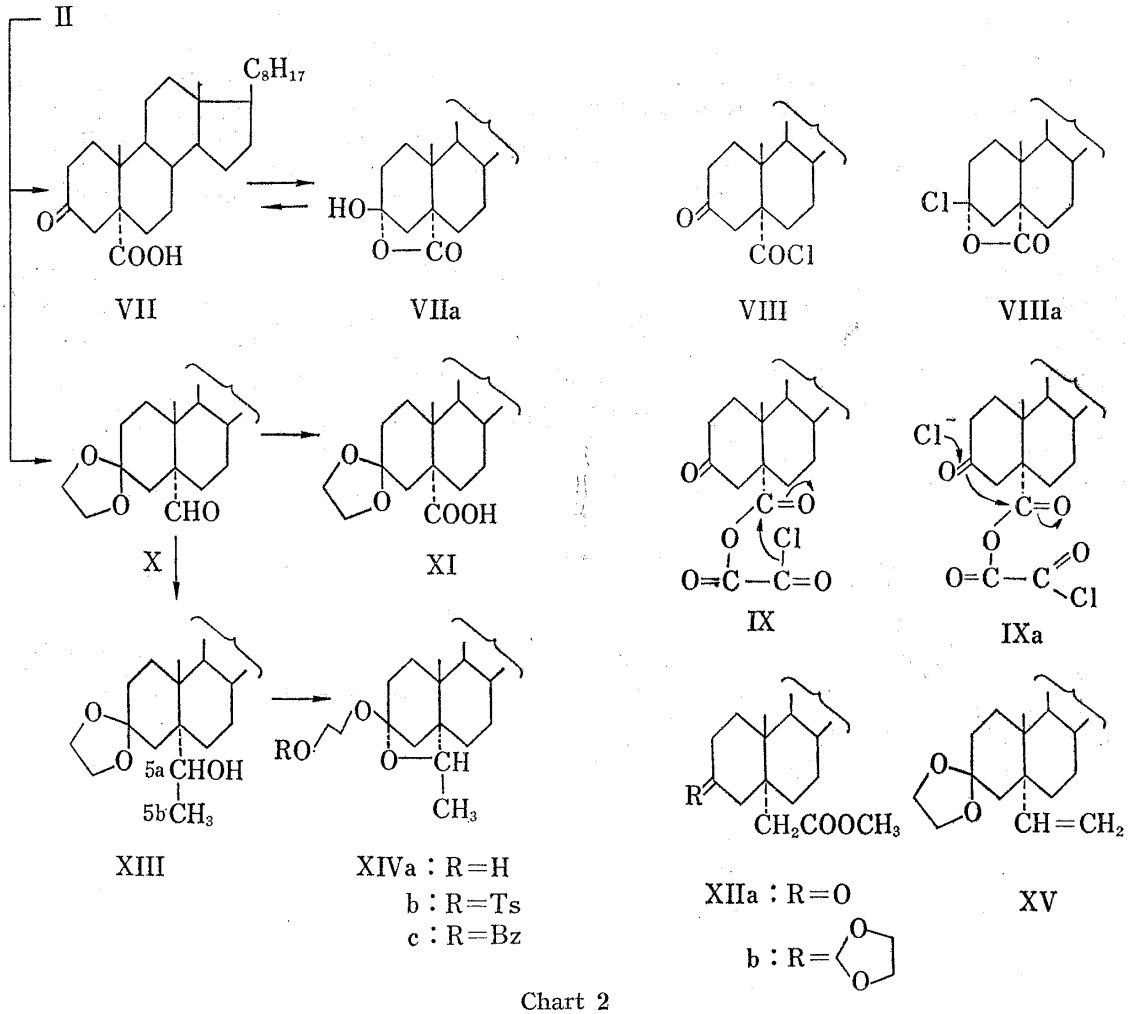

Chart 2

of the bridged chloride (VIIIa) as indicated by the presence of a γ-lactone band at 1772 cm^{-1} in the infrared. This fact can be explained by assuming that a transition state such as IXa may be more preferable than the normal one (IX). For avoiding such a participation of the 3-keto group, the sodium salt of the ketal carboxylic acid (XI), obtained from the aldehyde[7] (X) by potassium permanganate oxidation, was treated successively with oxalyl chloride, dia-

4) W. Nagata and M. Narisada, *Chem. Pharm. Bull.* (Tokyo), **16**, 867 (1968).
5) W. Nagata, S. Hirai, H. Itazaki, and K. Takeda, *Liebigs Ann. Chem.*, **641**, 184 (1961).
6) *cf.* A.L. Wilds and C.H. Schunk, *J. Am. Chem. Soc.*, **70**, 2427 (1948).
7) W. Nagata, S. Hirai, H. Itazaki, and K. Takeda, *Liebigs Ann.*, **641**, 196 (1961).

zomethane, and silver oxide. However, none of the desired homo-carboxylic acid methyl ester (XIIb) was formed. We next examined a possible route starting from the ketal aldehyde (X). Methyllithium was found to be efficient enough to react with the considerably inert, angular formyl group. Thus, treatment of X with this reagent smoothly gave the methyl carbinol (XIII). The desired two-carbon chain was thus formed at the 5α-position. To transport the hydroxyl group from the 5a- to the 5b-position of the ethyl side chain, initial removal of this group is necessary. An attempt to obtain the olefin (XV) *via* the 5a-tosylate of the secondary alcohol (XIII) was unsuccessful. The tosylate obtained was found to be the primary one (XIVb), as suggested by its stability to the elimination reaction. If it were the desired secondary tosylate, it should have been easily eliminated because of its neopentyl type structure. Similarly, benzoylation of XIII with benzoyl chloride in pyridine at 70—80° gave an oily bridged ketal benzoate (XIVc), pyrolysis of which recovered a greater part of the unchanged material. Whereas the ketal (XIII) showed a sharp signal at 6.00τ corresponding to four protons, the tosylate (XIVb) and the benzoate (XIVc) showed an A_2B_2 type signal at about 5.8 and 6.3τ and 5.60 and 6.01τ, respectively, in the NMR spectra. This fact indicates non-equivalency of the two methylene protons and therefore the validity of the assigned structure. The structure was confirmed by hydrolysis of the benzoate with aqueous alkali to the other ketal (XIVa). Since this ketal was also obtained from the normal ketal (XIII) by heating with aqueous acetic acid, the bridged form (XIVa) should be assigned to this newly formed ketal. The observed abnormal acylation unquestionably arose from the reluctance of the secondary hydroxyl group to the reagent because of its highly hindered character. The marked facility of this acid-induced transetherification has very often been observed in this laboratory and can be explained reasonably by release of a high compression energy contained in the molecule of the normal ketal (XIII).

The above results suggest that it is wise to utilize the acetoxy mesylate (XVI) in which the 5a-hydroxyl group is already mesylated. The seven-step synthesis of this compound from II was already reported in the preceding paper.[1] It did not appear difficult to convert compound (XVI) into the 5α-vinyl compound (XV) by applying the fragmentation reaction.[8] Actually, refluxing of an aqueous methanolic dioxane solution of XVI gave the vinyl ketone (XVII) in 74% yield under the 1,6-type fragmentation[8] as illustrated in XVIII. Compound (XVII) showed vinyl bands at 3099, 1636, 1004, and 924 cm^{-1} and a six-membered ring ketone band at 1713 cm^{-1} in the infrared, and the same strong positive Cotton effect in the ORD curve as that [7] for 5α-methylcholestan-3-one. These results support the assigned structure. When the fragmentation reaction was carried out in a more polar solvent system,[9] the yield of XVII was markedly reduced and a considerable amount of undesired by-products such as the olefin (XIX) and the diol (XX) were formed. This fact indicates that the concerted process becomes unfavorable with the increasing polarity of the solvent and as a result the 1,2-elimination and substitution products increase. The vinyl ketone (XVII) was converted into the vinyl ketal (XV), an important intermediate for the present purpose. Anti-Markownikoff hydroxylation of this compound using Brown's hydroboration process[10] gave either the normal hydroxy ketal (XXI) or the bridged hydroxy ketal (XXIIa) depending upon the experimental conditions.[9] Though of similar melting points, both compounds can be well differentiated by comparison of their IR spectra or thin-layer chromatograms. The same hydroxy ketone (IIIa) was obtained by deketalization of XXI or XXIIa. The assignment of the bridged form to the latter compound is based on the fact that the acetyl group of the acetate (XXIIb) derived from XXIIa was lost by treatment with aqueous acetic acid (70%). That this treatment does not cause hydrolysis of the acetoxyl group has been proven in a similar case.[3]

8) C.A. Grob, *Experientia*, **13**, 126 (1957).
9) See experimental part.
10) H.C. Brown and B.C. Subba Rao, *J. Am. Chem. Soc.*, **81**, 6428 (1959).

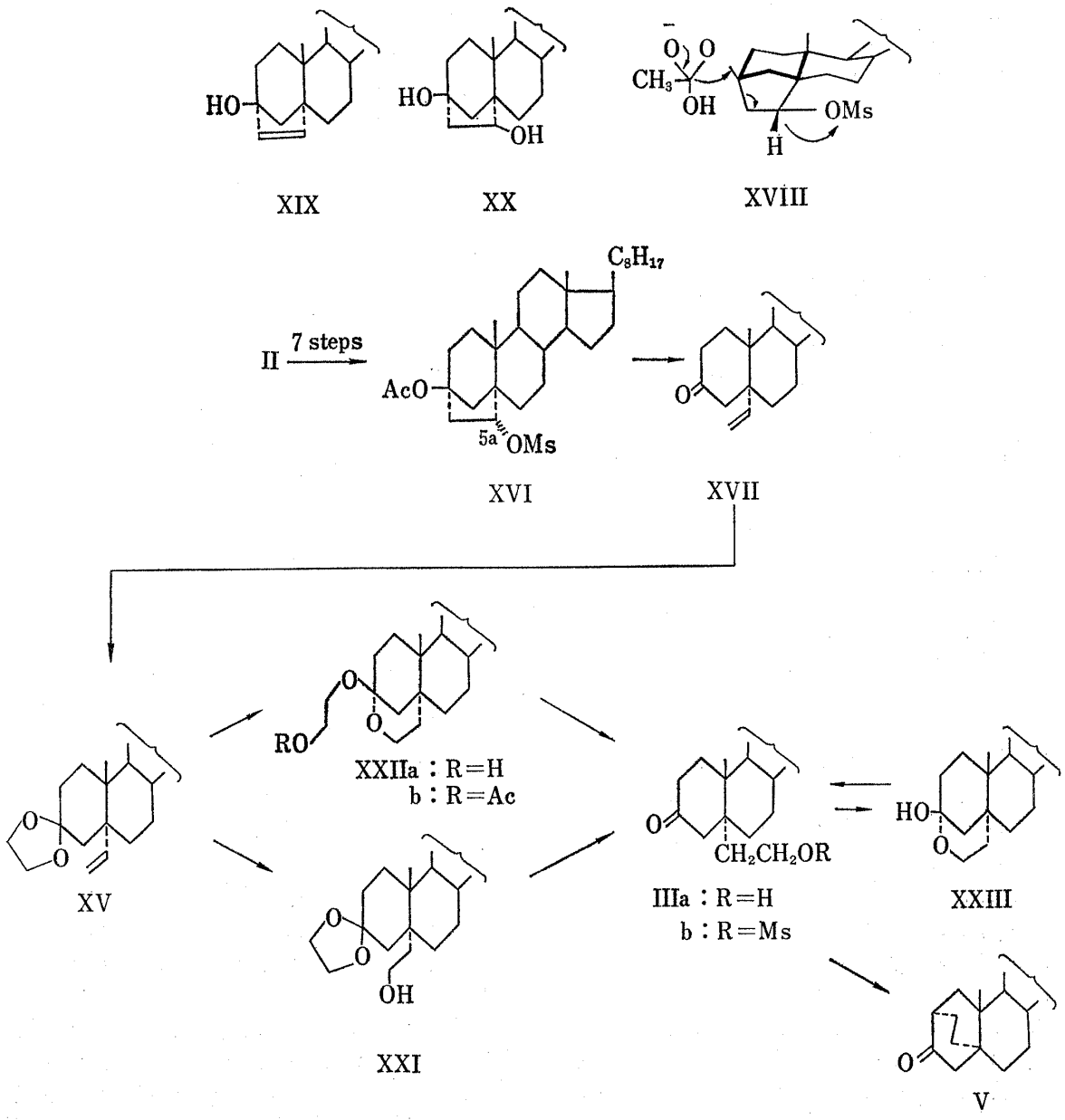

Chart 3

Although the hydroxy ketone (IIIa) exists, to some extent, as an equilibrium mixture with the isomeric bridged hemiketal (XXIII) in solution as judged by a weakened carbonyl band in the infrared and a reduced amplitude in the ORD curve,[9] the sole product obtained in 86% yield by the usual mesylation process was found to be the keto mesylate (IIIb). This compound was smoothly cyclized by treatment with potassium *tert*-butoxide in *tert*-butanol to the pentacyclic ketone (V) in 86% yield. The structure of this compound was confirmed by a six-membered ring carbonyl band at 1728 cm^{-1} in the infrared and a weak negative Cotton effect[11] in the ORD curve. The 3-keto group in this compound is suitable for introducing an allylic alcohol function of the atisine type (*vide infra*).

An alternative route leading to this key compound (V) starting from the bridged compound (XVI) was also established. As already described in the preceding paper,[1] XVI was transformed into the keto aldehyde (XXVI) *via* the olefin (XXIV) and the 1,2-diol (XXV) by successive treatment of XVI with collidine, bis(3-methyl-2-butyl)borane, alkaline hydrogen

11) For related compounds see L.H. Zalkow and N.N. Girotra, *J. Org. Chem.*, **29**, 1299 (1964).

peroxide, potassium hydroxide, and periodic acid. The keto aldehyde (XXVI) was readily cyclized with diluted alkali to the bridged ketol (VIa). The ORD curve of this compound showed a weak negative Cotton effect similar to that observed for the desoxy derivative (V). The ketol (VIa) was then converted into the keto olefin (XXVIII) by refluxing the mesyl derivative (VIb) of the former with collidine. The bridged keto olefin (XXVIII) showed a strong positive Cotton effect in the ORD curve in good coincidence with the observation of

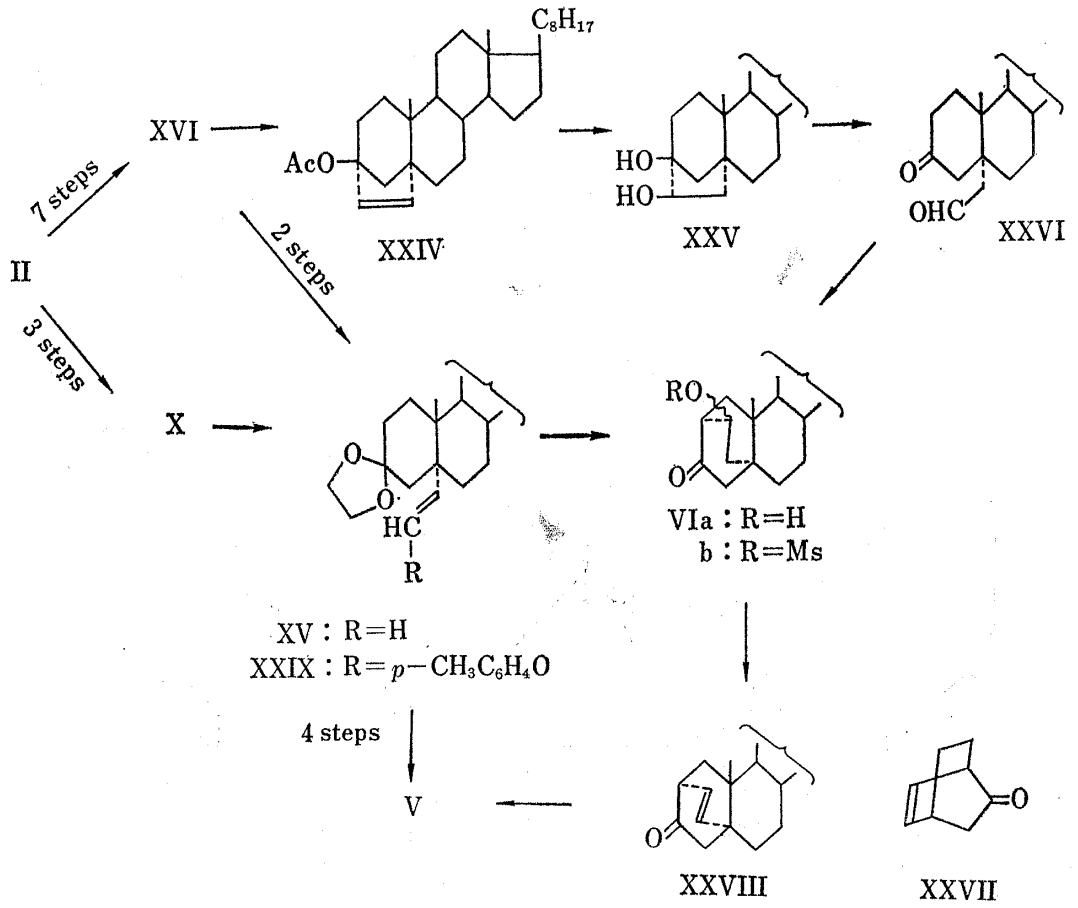

Chart 4

Moscowitz, *et al.*[12] and Mislow and Berger[13] who reported a strong negative Cotton effect for the bicyclo[2.2.2]octenone having the absolute configuration as depicted in formula (XXVII). The keto olefin was converted finally into the pentacyclic ketone (V) by catalytic hydrogenation.

We next examined the third route, the simplest one. Before exploring the first and second routes, we examined the Wittig condensation reaction[14] on the ketal aldehyde (X). Unfortunately, an initial attempt failed probably because of improper experimental conditions. Reexamination carried out after establishment of the other two routes showed this olefination reaction was quite successful.[15] Thus, the ketal aldehyde (X) was smoothly converted into the corresponding olefin (XV) or (XXIX) by treatment with methylene[14] or *p*-tolyloxymethylenetriphenylphosphorane[16] in good yield. Product (XV) was proven to be identical with a sample obtained by the first route. The *p*-tolyloxy olefin (XXIX) was then treated with perchloric acid giving the bridged ketol (VIa). The intermediate of this cycli-

12) A. Moscowitz, K. Mislow, M.A.W. Glass, and C. Djerassi, *J. Am. Chem. Soc.*, **84**, 1945 (1962).
13) K. Mislow and J.G. Berger, *J. Am. Chem. Soc.*, **84**, 1956 (1962).
14) G. Wittig and V. Schollkopf, *Chem. Ber.*, **87**, 1318 (1954).
15) For the related examples see; O. Halpern, R. Villotti, and A. Bowers, *Chem. Ind.* (London), **1963**, 116; J.A. Edwards, M.C. Calzada, L.C. Ibanez, and A. Bowers, *Steroids*, **6**, 371 (1965).
16) G. Wittig, W. Böll, and K.H. Krück, *Chem. Ber.*, **95**, 2514 (1962).

zation is probably the keto aldehyde (XXVI), although this compound could not be isolated. The over-all yield of the bridged ketol (VIa) from the ketal aldehyde (X) was 61%.

Finally, investigations for introducing the allylic alcohol function of the atisine type into the bridged ring system of V are described. The pentacyclic ketone (V) was converted by the usual method[17] into the epoxy acetate (XXX) which, without purification, was transformed into the *cis* glycol (XXXII) either *via* the ketol (XXXI) or directly by treatment with methylmagnesium iodide in an over-all yield of 15% or 19% from V. The same glycol (XXXII) was also obtained by osmium tetroxide oxidation of a 10:3 mixture of the *endo* and the *exo* olefins, (XXXIV) and (XXXIII). This olefin mixture was formed by an acid-catalyzed equilibration of a 5:6 mixture obtained from the ketone (V) by the Grignard reaction and subsequent dehydration with phosphorus oxychloride. The course of isomerization of the *exo* to the *endo* double bond was followed by a decreasing band intensity at 877 cm^{-1} characteristic of the former in the infrared, and the proportion of both the olefins was determined by gas-liquid chromatography. By this route, the *cis*-diol (XXXII) was obtained in 28% over-all yield from the ketone (V) in preference to the yield in the route *via* the epoxy acetate.

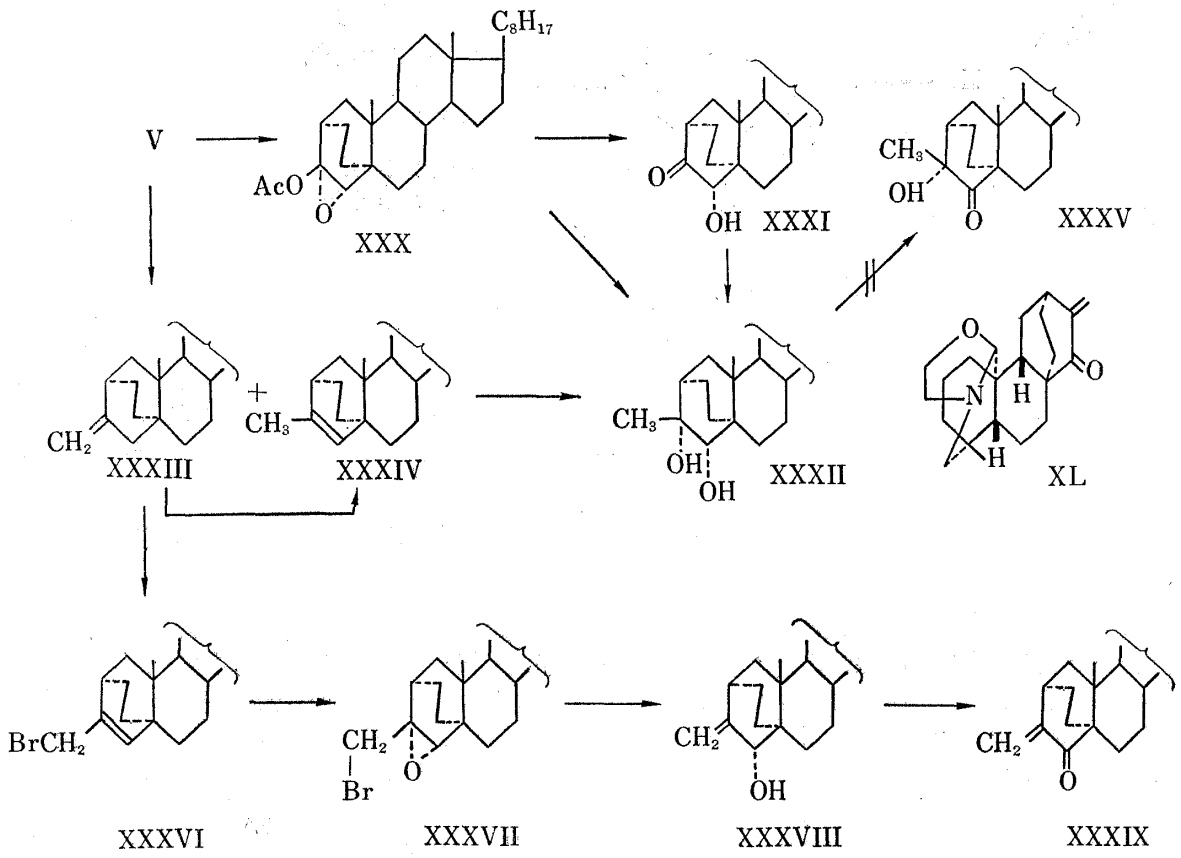

Chart 5

The configuration of the hydroxyl groups in the *cis*-diol (XXXII) was assigned as α by analogy with the allylic alcohol (XXXVIII) (*vide infra*). This assignment is also supported by assuming that osmium tetroxide or perbenzoic acid attacks the substrate from the α-side avoiding the bulky 19-methyl group. Unfortunately, an attempt to convert the *cis*-diol (XXXII) into the ketol (XXXV) by oxidation with chromic anhydride in acetic acid or in pyridine failed because of occurrence of the facile cleavage reaction giving a large amount of acidic products.

17) *cf.* J. Fishman and T. Nambara, *J. Org. Chem.*, **27**, 2131 (1962).

The pentacyclic ketone (V) was next treated with methylene triphenylphosphorane[14] giving the *exo* olefin (XXXIII) in 91% yield. Wohl–Ziegler bromination[18] of this olefin with N–bromosuccinimide in refluxing carbon tetrachloride in the presence of benzoyl peroxide gave the rearranged allylic bromide (XXXVI) in 71% yield. The same bromide was also obtaind by the same treatment of the 3:10 equilibrium mixture of the *exo* and the *endo* olefins, (XXXIII) and (XXXIV), as described above. The formation of XXXVI as a sole product indicates that a resonance–stabilized allyl radical is attacked by the bromine radical at the less hindered primary carbon. The structural assignment of the allylic bromide (XXXVI) is based on the signals at 4.15τ and 6.01τ corresponding to one olefinic and two allylic protons, respectively, in the NMR spectrum and the absence of the bands responsible for the *exo* methylene in the infrared. Compound (XXXVI) was oxidized with perbenzoic acid to give the epoxy bromide (XXXVII) which, without purification, was treated with zinc in refluxing ethanol giving the allylic alcohol (XXXVIII). This compound was obtained from the *exo* olefin (XXXIII) in an over–all yield of 53% by three steps, when the reactions were carried out without purification of the intermediates. The structural assignment was based upon the IR bands at 3635 cm^{-1} and at 3071, 1657, and 902 cm^{-1} responsible for a hydroxyl and a vinyl group, respectively, and upon the signals at 5.01τ corresponding to two geminal olefinic protons in the NMR spectrum. The 4α–configuration of the allylic hydroxyl group is deduced from the fact that a small up–field shift of 2.5 cps for the 19–methyl signal of the allylic alcohol (XXXVIII) as compared with that of the starting *exo* olefin (XXXIII) cannot be expected for the 4β–hydroxy epimer which should show a marked down–field shift of about 15 cps for the 19–methyl signal arising from the 1,3 diaxial relation of the hydroxyl and the methyl groups.[19] This assignment is quite reasonable from the same reason discussed in the case of the *cis*–diol (XXXII). Thus, synthesis of the cholestane derivative having the same moiety as the C–D ring part of atisine, except for the configuration of the allylic hydroxyl group, was attained. Compound (XXXVIII) was further oxidized to the conjugated enone (XXXIX) which showed bands at 1711 and 1637 cm^{-1} in the infrared and an absorption at 228 mμ (ε=5970) in the ultraviolet, both responsible for a conjugated enone system in good coincidence with the reported values[20] of 1702 and 1638 cm^{-1} in the infrared and of 228 mμ (ε=9100) in the ultraviolet for the enone (XL) derived from atisine (I).

Experimental

An Attempted Synthesis of Methyl 3-Oxocholestan-5α-ylacetate (XIIa)——Compound (VII)[5] (303 mg, 0.704 mmoles) dissolved in dioxane was neutralized with 0.106 N NaOH (6.70 ml, 0.707 mmoles), and the sodium salt formed was lyophyrized and then dried at 100—130° and 0.005 mmHg. To a suspension of the VII–Na–salt (IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1698 (C=O), 1585 (broad, COO^-)) in anhydrous benzene (10 ml) was added oxalyl chloride (1.9 g, 15 mmoles) dropwise with ice–cooling. The resulting mixture was stirred for 5 min, mixed with pyridine (2 drops), and kept at 0° for 10 min and then at room temperature for another 20 min. An insoluble material was removed by filtration and the filtrate was concentrated to dryness under reduced pressure, and the last traces of the solvent were removed by codistillation with benzene. The residue (VIIIa) was dissolved again in anhydrous benzene (5 ml), and the solution was added dropwise at −15° to an ethereal solution (25 ml) of diazomethane (prepared from 3 g of nitrosomethylurea, and dried with KOH and Na wire). The resulting mixture was allowed to stand for 1 hr at this temperature, for 30 min at 0°, and then for 35 hr at room temperature. The IR spectrum of the product obtained by the usual work–up was nearly superimposable with that of VIIIa ($\nu_{max}^{CHCl_3}$ cm^{-1}: 1772) and showed no band of the diazoketone grouping.

3,3-Ethylenedioxy-5α-carboxylcholestane (XI)——A mixture of the ketal aldehyde (X)[6] (2.000 g), acetone (100 ml), and $KMnO_4$ (828 mg, 1.2 molar equiv.) was refluxed for 15 min. The reaction mixture was concentrated almost to dryness and the residue was dissolved in 2% KOH and $CHCl_3$. The mixture was filtered through a celite layer to remove an insoluble material, which was washed with MeOH. The

18) *cf.* L. Horner and E.H. Winkelmann, *Angew. Chem.*, **71**, 349 (1959).
19) T. Okamoto and Y. Kawazoe, *Chem. Pharm. Bull.* (Tokyo), **11**, 643 (1963).
20) S.W. Pelletier and W.A. Jacobs, *J. Am. Chem. Soc.*, **76**, 4496 (1954).

filtrate and the washings were combined, acidified with dil. HCl, and extracted with $CHCl_3$. The $CHCl_3$ layer was washed with H_2O, dried over Na_2SO_4 and evaporated *in vacuo*. The residue (2.001 g) was chromatographed on silica gel (30 g). Fractions eluted with benzene:$CHCl_3$ (4:1) were recrystallized from CH_2Cl_2–MeOH to give XI (598 mg, 29%), mp 191—191.5°. An analytical sample melts at mp 190—191°. *Anal.* Calcd. for $C_{30}H_{50}O_4$: C, 75.90; H, 10.62. Found: C, 76.27; H, 10.49. IR ν_{max}^{Nujol} cm^{-1}: 3238, 1737, 1142. $[\alpha]_D^{26.5}$ +34.0±2° ($CHCl_3$, c=1.077).

The residue from the mother liquor was dissolved in ether:$CHCl_3$ (3:1) and treated with 2 N KOH to separate an acid substance (713 mg) and a neutral one (490 mg). The former gave crystals of mp 176—179° (433 mg), which was not investigated further.

An Attempted Synthesis of Methyl 3,3-Ethylenedioxycholestane-5-ylacetate (XIIb)——Compound (XI) (501 mg) dissolved in dioxane (10 ml) was neutralized with 0.50 N NaOH (2.11 ml), and the sodium salt was lyophyrized and then dried for 2 hr at 110° and 0.01 mmHg. To a suspension of the XI–Na–salt in anhydrous benzene (12 ml) containing pyridine (3 drops), oxalylchloride (2.0 ml) was added with ice–cooling, and the mixture was shaken for 4 min. The reaction mixture was concentrated to dryness *in vacuo* and the last traces of the solvent was removed by codistillation with anhydrous benzene. The residue was dissolved in anhydrous benzene, and the insoluble part was removed by filtration and washed with anhydous benzene. The filtrate and the washing were combined and mixed with anhydrous ether (5 ml). The resulting mixture was added dropwise with stirring at −15° to an ethereal diazomethane solution (prepared from nitrosomethylurea (7 g) and dried over KOH), and the mixture was kept −15° for 90 min and at room temperature for 90 min. Concentration of the reaction mixture gave a residue (530 mg), IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2148, 1648 (diazoketone), 1822, 1743, 1719 (weak). To the residue dissolved in MeOH (25 ml) and dioxane (25 ml) was added at 55—60° Ag_2O (prepared from 10% $AgNO_3$ (2 ml) and NaOH) in 4 portions over a period of 1 hr. After the same amount of Ag_2O was added at one time the mixture was refluxed for 20 min, poured into ice–water, and extracted with ether. The ether layer was washed with 2 N KOH, H_2O, dried over Na_2SO_4, and evaporated. The residue (404 mg) was chromatographed on neutral Al_2O_3 (15 g). Fractions eluted with petroleum–ether and benzene (2:1)—(1:1) were recrystallized from ether–pentane to give 5α–carbomethoxycholestan–3–one (58 mg, 12%), mp 146—149°, which was proved to be identical with an authentic sample by the mixed melting point and comparison of IR–spectra. Fractions eluted with benzene:$CHCl_3$ (1:1) on recrystallization from CH_2Cl_2–MeOH gave crystals (38 mg, mp 130—131°). *Anal.* Calcd. for $C_{32}H_{54}O_4$: C, 76.44; H, 10.83. Found: C, 75.18; H, 10.62. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3542 (OH), 1732, 1711. Fractions eluted whith benzene–$CHCl_3$ (4:1) on recrystallization from CH_2Cl_2–MeOH gave crystals (4 mg, mp 205—215°). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1720. Structures of the crystals of mp 130—131° and of mp 205—215° were not investigated.

3,3-Ethylenedioxy-5α-(1-hydroxyethyl)cholestane (XIII)——To X (5.679 g) dissolved in anhydrous ether (57 ml), 1.59 N ethereal CH_3Li (39 ml, 5 molar equiv.) was added dropwise with ice–cooling and stirring under nitrogen, and the mixture was kept for 3 hr under the same conditions. The mixture was poured into ice–water and extracted with ether. Washing of the ether layer with H_2O, drying over Na_2SO_4, and concentration gave a residue (5.87 g). The residue (4.17 g) was chromatographed on neutral Al_2O_3 (75 g). Fractions (3.376 g, 81%) eluted with petroleum ether–benzene (9:1) crystallized (mp 79—86°) on standing in a refrigator for a weak. The crystals were recrystallized twice from acetone–MeOH to give an analytical sample of XIII melting at 91—92°. *Anal.* Calcd. for $C_{31}H_{54}O_3$: C, 78.42; H, 11.47. Found: C, 78.07; H, 11.41. $[\alpha]_D^{23.5}$ −3.6±2° ($CHCl_3$: c=1.06%). IR $\nu_{max}^{CCl_4}$ cm^{-1} (0.076 mmole/liter) cm^{-1}: 3490 (intramolecular hydrogen bond). NMR (in $CHCl_3$) τ: 6.02 (singlet, 4H). Fractions eluted with petroleum ether:benzene (4:1) were recrystallized from CH_2Cl_2–MeOH and then acetone to give crystals (59 mg, mp 157—159°), which was not further investigated. A pure sample melts at 158—163°. *Anal.* Calcd. for $C_{32}H_{56}O_3$: C, 78.63; H, 11.55. Found: C, 78.71; H, 11.47. IR no OH band. $[\alpha]_D^{23.5}$ +5.5±2° ($CHCl_3$: c=1.010).

3β-(2-Tosyloxyethoxy)-5a-methyl-3α,5α-epoxymethanocholestane(XIVb)——The methylhydrin(XIII)(351 mg) dissolved in anhydrous pyridine (7 ml) was mixed with tosyl chloride (706 mg) with ice–colling, and the mixture was allowed to stand for 15 hr at room temperature. Ice was added, and the resulting mixture was stirred for 1 hr at room temperature to decompose excess tosyl chloride, mixed with ether:$CHCl_3$ (3:1), and poured into 2 N HCl–ice–water. After separation of the organic layer, the 2 N HCl layer was extracted further with ether. The combined organic layers were washed with H_2O, dried, and concentrated *in vacuo* to afford a residue (349 mg). Successive recrystallization from MeOH and CH_2Cl_2–MeOH gave XIVb (100 mg, 22%), mp 140—141°. *Anal.* Calcd. for $C_{38}H_{60}O_5S$: C, 72.57; H, 9.62; S, 5.10. Found: C, 72.30; H, 9.64; S, 5.00. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1602, 1360, 1175. NMR (in $CHCl_3$) τ: 5.8, 6.3 (4H, A_2B_2 type).

3β-(2-Benzoyloxyethoxy)-5a-methyl-3α,5α-epoxymethanocholestane (XIVc)——The methylhydrin (XIII) (695 mg) dissolved in anhydrous pyridine (17 ml) was mixed with benzoyl chloride (2.06 g), and the mixture was heated at 70—80° for 4 hr. The reaction mixture was worked up in a similar manner to that described for XIVb to give a crude sample of (XIVc) (845 mg), which did not crystallize. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1724, 1605. NMR (in $CHCl_3$) τ: 5.60, 6.10 (5H).

Alkaline Hydrolysis of XIVc——A mixture of XIVc (85 mg), 2 N KOH (3 ml), EtOH (20 ml), and dioxane (10 ml) was refluxed for 2 hr. The mixture was concentrated, diluted with H_2O, and extracted with ether. Washing of the ether–layer, drying over Na_2SO_4, and concentration gave a residue (60 mg), which was recrystallized from acetone to afford XIVa (29 mg), mp 111—112°. For physical data see below.

Acid Treatment of XIII——A solution of XIII (200 mg) in 80% HOAc (12.5 ml) was heated at 100° for 30 min. The reaction mixture was worked up in the same way as described above to give XIVa (100 mg, 50%), mp 109—111° (from acetone), whose mixed melting point with XIVa obtained from XIVc showed no depression. IR-spectra of both the samples were also superimposable. A pure sample melts at 113—115°. *Anal.* Calcd. for $C_{31}H_{54}O_3$: C, 78.42; H, 11.47. Found: C, 78.57; H, 11.39. IR $\nu_{max}^{CCl_4}$ cm^{-1}: (dilute solution): 3605, 3460. NMR (in $CHCl_3$) τ: 6.30 (singlet 4H).

5α-Vinylcholestan-3-one (XVII)——A mixture of mesyl acetate (XVI)[1] (1.861 g), KOH (6 g), dioxane (28 ml), MeOH (40 ml), and H_2O (8 ml) was refluxed for 2 hr in a nitrogen atmosphere. The mixture is concentrated, diluted with H_2O, and extracted with ether. The ether layer was washed with H_2O, dried over Na_2SO_4, and evaporated. The residue was recrystallized from ether–MeOH to give XVII (1.023 g, 74%), mp 135—141°. A pure sample melts at 144—145°. *Anal.* Calcd. for $C_{27}H_{48}O$: C, 84.41; H, 11.72. Found: C, 84.74; H, 11.68. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3099, 1636, 1004, 924 (–CH=CH_2), 1713 (C=O). ORD $[\phi]_{272\,m\mu}^{29}$ −2750, $[\phi]_{312\,m\mu}^{27}$ +2820, $[\phi]_{317\,m\mu}^{27}$ +2930 (dioxane, c=0.528).

Ketalization of XVII——A solution of XVII (413 mg), ethyleneglycol (0.12 ml) and *p*-toluenesulfonic acid (8 mg) in anhydrous benzene (15 ml) was distilled slowly to remove water as an azeotropic mixture under simultaneous addition of anhydrous benzene (10 ml) over a period of 3.5 hr. The solution was concentrated to 5 ml, poured into 2 N Na_2CO_3 with ice-cooling, and extracted with ether. Washing of the ether-layer with H_2O, drying, and evaporation gave a residue, which was recrystallized from ether–MeOH to give XV (403 mg, 88%), mp 90.5—91.5°. *Anal.* Calcd. for $C_{31}H_{52}O_2$: C, 81.52; H, 11.48. Found: C, 81.31; H, 11.25. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3068, 1628, 992, 907, 1081.

3,3-Ethylenedioxy-5α-(2-hydroxyethyl)cholestane (XXI)——Into a solution of XV (864 mg) in anhydrous tetrahydrofuran (10 ml), diborane gas (prepared from $BF_3 \cdot Et_2O$ (2.33 ml) in anhydrous diglyme (5 ml) and $NaBH_4$ (316 mg) in anhydrous diglyme (6 ml)) was introduced with stirring under nitrogen at 0° during 1 hr. The diborane generator was warmed to expel the diborane gas dissolved in diglyme when evolution of the gas almost subsided. The reaction mixture was stirred at room temperature for 2.5 hr and mixed successively with H_2O (1.85 ml), 3 N NaOH (3.7 ml), and 30% H_2O_2 (3.7 ml) with ice-cooling. Tetrahydrofuran (10 ml) and 1.5 N NaOH (4 ml) were added thereto, and the mixture was stirred for 1 hr at room temperature. Extraction with ether:$CHCl_3$ (3:1) and the usual work-up of the extract gave a residue (829 mg), which was chromatographed on neutral Al_2O_3 (30 g). Fractions eluted with benzene were recrystallized from ether to give XXI (199 mg, 26%), mp 134.5—135°. *Anal.* Calcd. for $C_{31}H_{54}O_3$: C, 78.42; H, 11.47. Found: C, 78.64; H, 11.40. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3619, 1086.

3β-(2-Hydroxyethoxy)-3α,5α-epoxyethanocholestane (XXIIa)——Through a solution of XV (5.568 g) in anhydrous tetrahydrofuran (30 ml) was bubbled with ice-cooling under N_2 diborane gas prepared from $BF_3 \cdot Et_2O$ (3.95 ml) and $NaBH_4$ (1.39 g) and dried by passing through a trap cooled at −10～−15°. The resulting mixture was allowed to stand for 1 hr at room temperature. After the successive addition of H_2O, 3 N NaOH (15 ml), and 30% H_2O_2 (15 ml) with ice-cooling and stirring, the mixture was stirred for 50 min at room temperature. Extraction with ether:$CHCl_3$ (3:1) and the usual work-up of the extract gave a residue (5.86 g), which was chromatographed on neutral Al_2O_3 (250 g). Fractions eluted with petroleum ether:benzene (4:1) gave the starting material (XV) (385 mg), mp 88—90.5°. Fractions eluted with petroleum ether:benzene (2:1) gave XVII (10 mg), mp 133—140°. Fractions eluted with benzene:$CHCl_3$ (4:1) were recrystallized from ether:MeOH to give XXIIa (2.941 g, 51%), mp 134—134.5°. A pure sample melts at 133—134°. *Anal.* Calcd. for $C_{31}H_{54}O_3$: C, 78.42; H, 11.47. Found: C, 78.64; H, 11.37. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3606, 3416, 1073.

5α-(2-Hydroxyethyl)cholestan-3-one (IIIa)——a) Deketalization of XXI: A mixture of XXI (197 mg), 2 N HCl (1 ml), and dioxane (5 ml) was heated at 100° for 1.5 hr. The mixture was poured into ice-water and extracted with ether:$CHCl_3$ (3:1). The organic layer was washed with H_2O, dried with Na_2SO_4, and evaporated. The residue was recrystallized from CH_2Cl_2–acetone to give IIIa (155 mg, 87%), mp 176.5—178°. A pure sample melts at 177—178.5°. *Anal.* Calcd. for $C_{29}H_{50}O_2$: C, 80.87; H, 11.70. Found: C, 81.08; H, 11.71. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3598, 1699 (weak), 1177. ORD $[\phi]_{279m\mu}^{26}$ −720, $[\phi]_{315m\mu}^{26}$ +1180 (Dioxane, c=0.318). $[\alpha]_D^{22}$ +20.0±2° ($CHCl_3$: c=1.077).

b) Deketalization of XXIIa: Compound (XXIIa) (2.745 g) dissolved in dioxane (75 ml) was treated with 2 N HCl (15 ml) in the same manner as that described in a). The crystals obtained (2.279 g, 92%) melted at 178—180°, whose mixed melting point with IIIa obtained above showed no depression. Their IR-spectra were also superimposable.

c) Acetylation of XXIIa to XXIIb and hydrolysis of XXIIb to IIIa: A mixture of XXIIa (56 mg), dry pyridine (1 ml), and Ac_2O (0.3 ml) was let stand overnight at room temperature. The mixture was poured into ice-water and extracted with CH_2Cl_2. The CH_2Cl_2-layer was washed successively with 1 N HCl, H_2O, 2 N Na_2CO_3, and H_2O, dried with Na_2SO_4, and evaporated. Recrystallization of the residue from ether: MeOH gave XXIIb (51 mg, 83%), mp 88—89°. *Anal.* Calcd. for $C_{33}H_{56}O_4$: C, 76.69; H, 10.92. Found: C, 76.80; H, 10.99. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1734.

A solution of XXIIb (31 mg) in 75% HOAc (3 ml) was heated at 100° for 20 min. After concentration *in vacuo*, the reaction mixture was extracted with CH_2Cl_2, and the organic layer was washed with 2 N Na_2CO_3 and H_2O, dried, and evaporated. Recrystallization of the residue from acetone gave IIIa (21 mg), mp

178—180.5°, which was proved to be identical with the sample of IIIa obtained above by comparison of their IR-spectra and mixed melting point measurement.

5α-(2-Hydroxyethyl)cholestan-3-one Mesylate (IIIb)——A solution of IIIa (245 mg) in dry pyridine (8 ml) was mixed with mesylchloride (0.22 ml), and the mixture was allowed to stand overnight at room temperature. The mixture was mixed with a small amount of ice and stirred for 1 hr to decompose excess mesyl chloride and poured into a mixture of 2 N HCl (80 ml) and ice. The mixture was extracted with $CHCl_3$:ether (3:1), and the organic layer was washed with H_2O, dried, and evaporated. The residue was recrystallized from CH_2Cl_2–acetone to give IIIb (248 mg, 86%), mp 180—181°. A pure sample melts at 179—180°. *Anal.* Calcd. for $C_{30}H_{52}O_4S$: C, 71.10; H, 9.95; S, 6.33. Found: C, 71.01; H, 10.15; S, 6.45. $[\alpha]_D^{24}$ +33.8±2° ($CHCl_3$: c=1.059). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1704, 1363, 1170. ORD $[\phi]_{273\,m\mu}^{27}$ −2690, $[\phi]_{318\,m\mu}^{27}$ +3720 (dioxane, c=0.300).

2α,5α-Ethanocholestan-3-one (V) from Ketolmesylate (IIIb)——To IIIb (195 mg) dissolved in t-BuOH (10 ml), 1 N solution of t-BuOK in t-BuOH (1.2 molar equiv.) was added dropwise with stirring under nitrogen at room temperature, and the colloidal mixture was stirred for 2 hr. It was diluted with ice–water and extracted with ether. The ether layer was washed with H_2O, dried, and evaporated. Recrystallization of the residue from ether–MeOH gave V (136 mg, 86%), mp 84—85°. The physical constants are shown later.

2α,5α-Ethanocholestan-2α-ol-3-one (VIa)——To XXVI[1] (100 mg) dissolved in MeOH (20 ml), 0.5 N KOH (20 ml) was added and the resulting suspension was stirred for 1 hr at room temperture under nitrogen. The mixture was poured into ice–water and extracted with ether. The ether-layer was washed, dried, and evaporated. Recrystallization of the residue from CH_2Cl_2–MeOH gave VIa (100 mg, 91%), mp 194.5—196°. A pure sample melts at 195—197°. *Anal.* Calcd. for $C_{29}H_{48}O_2$: C, 81.25; H, 11.29. Found: C, 81.48; H, 11.28. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3599, 3420, 1718. $[\alpha]_D^{24.5}$ +65.9±2° ($CHCl_3$, c=0.987). ORD $[\phi]_{288\,m\mu}$ +373, $[\phi]_{318\,m\mu}$ −160 (dioxane, c=0.293).

2α,5α-Ethenocholestan-3-one (XXVIII) *via* VIb——A mixture of VIa (146 mg), dry pyridine (1.5 ml), and mesyl chloride (0.13 ml) was let stand at room temperature for 2 days. The reaction mixture was poured into 2 N HCl–ice and extracted with ether:$CHCl_3$ (3:1). The usual work-up gave crude VIb (170 mg), which was refluxed with collidine (2 ml) for 8.5 hr in a nitrogen atmosphere. The reaction mixture was poured into 2 N HCl–ice and extracted with ether. The usual work-up of the ether layer gave a residue (129 mg), which was chromatographed on neutral Al_2O_3 (4 g). Fractions eluted with petroleum ether:benzene (9:1)—(2:1) were recrystallized from ether–MeOH to give XXVIII (86 mg, 63%), mp 85—90°. A pure sample melts at 86—94°. *Anal.* Calcd. for $C_{29}H_{46}O$: C, 84.81; H, 11.29. Found: C, 84.65; H, 11.00. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3052, 1731. UV ν_{max}^{EtOH} mμ (ε); 296 (136), $[\alpha]_D^{24.5}$ −143±2° ($CHCl_3$, c=1.058). ORD $[\phi]_{278\,m\mu}$ +22410; $[\phi]_{310\,m\mu}$ −18030; $[\phi]_{315\,m\mu}$ −15900; $[\phi]_{322\,m\mu}$ −27420 (dioxane, c=0.0656).

2α,5α-Ethanolchoestan-3-one (V) from XXVIII——Compound (XXVIII) (404 mg) dissolved in EtOH (15 ml) was hydrogenated in the presence of 10% Pd–carbon (16 mg) over a period of 7 hr. After removal of the catalyst, the filtrate was diluted with H_2O, extracted with ether. The ether layer was washed with H_2O, dried, and evaporated. Recrystallization of the residue from ether–MeOH gave V (29.4 mg, 73%), mp 86—87°. *Anal.* Calcd. for $C_{29}H_{48}O$: C, 84.40; H, 11.72. Found: C, 84.61; H, 11.76. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1728. $[\alpha]_D^{22.5}$ 725±4° ($CHCl_3$, c=0.603). ORD $[\phi]_{285\,m\mu}^{23}$ +3540; $[\phi]_{319\,m\mu}^{23}$ +270 (dioxane, c=0.259). NMR (in $CHCl_3$): 9.14 (3H, 19-Me).

Wittig Reaction of X to XV——To a stirred suspension of methyltriphenylphosphonium bromide (417 mg) in anhydrous ether (4 ml) was added dropwise 1.21 N ethereal solution of BuLi (0.90 ml, 1.09 mmoles) with ice-cooling under nitrogen. After the stirring was continued for 2 hr at room temperature, a solution of X (200 mg, 0.436 mmoles) in anhydrous tetrahydrofuran (5 ml) was added dropwise to the suspension, and the mixture was stirred for 2 hr at room temperature. It was poured into H_2O and extracted with ether. The usual work-up of the ether-layer gave a residue, which was chromatographed on Al_2O_3 (8g). Fractions eluted with petroleum ether were recrystallized from ether–MeOH to give XV (126 mg), mp 73—74°. From the mother liquor, an additional crop of XV (13 mg), mp 84—87°, was obtained. The total yield is 70%. A pure sample obtained by recrystallization of the sample melting at 73—74° shows 92—93°. $[\alpha]_D^{27.5}$ −10.2 ±2° ($CHCl_3$, c=1.029). The mixed mleting point of the first and the second crops showed 88—90°. The low melting point of the former is probably due to dimorphism. The IR-spectrum of XV of mp 73—74° is superimposable with that of XV obtained from XVII, and they show the same *Rf* values in their thin-layer chromatograms.

Wittig Reaction of X to 3,3-Ethylenedioxy-5α-(2-*p*-tolyloxyvinyl)cholestane (XXIX) and Subsequent Cyclization to VIa——To a stirred suspension of *p*-tolyloxymethyltriphenylphosphonium chloride (4.03 g, 7.25 mmoles) in anhydrous ether (15 ml) was added dropwise 1.08 N ethereal solution of BuLi (4.93 ml, 5.32 mmoles) at −5° under nitrogen, and the mixture was stirred at 0° for 5 min. To the resulting orange red ylid mixture was added dropwise a solution of X (666 mg, 1.45 mmoles) in anhydrous ether (25 ml) at −20°, and the mixture was sitrred for 1 hr at −20° and further for 1.5 hr at 0.° The reaction mixture was poured into ice–water and extracted with ether:$CHCl_3$ (3:1). The organic layer was washed with H_2O, dried and evaporated. The residue was chromatographed on Al_2O_3 (30 g). Fractions (908 mg) eluted with petroleum ether were further chromatographed on Al_2O_3 (25 g). The middle fractions eluted with petroleum ether

were recrystallized from ether–MeOH to give XXIX (111 mg), mp 151—154°. A pure sample melts at 161—162°. *Anal.* Calcd. for $C_{38}H_{58}O_3$: C, 81.09; H, 10.39. Found: C, 81.37; H, 10.31. $[\alpha]_D^{25.5}$ +37.2±4° ($CHCl_3$, c=0.538). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1656, 1611, 1588, 1503. The later part of the fractions (590 mg) eluted with petroleum ether (590 mg) did not crystallize, but its IR-spectrum is superimposable with that of XXIX of mp 151—154°. The total yield of the crude sample is 86%. A mixture of XXIX (mp 151—154°), ether (1.5 ml), benzene (0.3 ml), and 60% $HClO_4$ (0.58 ml) was heated with stirring at 70—80° for 1.5 hr. The mixture was neutralized with Na_2CO_3 (200 mg) and extracted with ether. The ether layer was washed with 2 N NaOH and H_2O, dried, and evaporated. The residue was recrystallized with CH_2Cl_2–MeOH to give VIa (27.3 mg, 80%), mp 193—195°. In the same way, VIa (314 mg), mp 195—196°, was obtained from the above oily sample of XXIX (590 mg). The total yield of VIa from X is 61%.

3α,4α-Epoxy-2α,5α-ethanocholestan-3β-ol Acetate (XXX)——A mixture of V (306 mg), *p*-toluenesulfonic acid (61 mg), and isopropenyl acetate (6.1 ml) was refluxed for 7 hr under nitrogen. The reaction mixture was mixed with NaOAc (0.12 g) and concentrated *in vacuo*. The residue was mixed with cold 1% $KHCO_3$, and the mixture was extracted with ether. The ether layer was washed with H_2O, dried, and evaporated to give a crude sample of the enol acetate (335 mg). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1764, 1729 (weak), 1671. The crude enol acetate (335 mg) was mixed with a 0.175 M solution of perbenzoic acid in $CHCl_3$ (6.0 ml), and the mixture was kept in the dark for 14 hr at room temperature. It was poured into ice-cold 2 N K_2CO_3 and extracted with ether. The organic layer was washed with H_2O, dried, and evaporated to give a crude sample of the epoxy acetate (XXX) (319 mg), which was used for the next reaction without purification. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1814 (weak), 1769, 1749, 1737 (shoulder), 1728.

2α,5α-Ethanocholestan-4α-ol-3-one (XXXI)——A mixture of the crude epoxy acetate (XXX) (348 mg), dioxane (30 ml), and 6 N H_2SO_4 (10 ml) was shaken in a closed flask for 18 hr at room temprature. The mixture was poured into ice–water and extracted with ether:$CHCl_3$ (3:1). The residue obtained by the usual work-up was chromatographed on silica gel (15 g). Fractions eluted with benzene:$CHCl_3$ (9:1)—(4:1) were recrystallized from ether–pentane to give XXXI (119 mg, 33%), mp 146—149°/159—159.5°. A pure sample melts at 144—146°/158—158.5° (double melting point). *Anal.* Calcd. for $C_{29}H_{48}O_2$: C, 81.25; H, 11.29. Found: C, 81.54; H, 11.42. $[\alpha]_D^{24.5}$ +13.2±2°($CHCl_3$, c=1.018). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3583, 1721. ORD:$[\phi]_{290\,m\mu}^{25}$ +3310, $[\phi]_{338\,m\mu}^{25}$ −2480 (dioxane, c=0.225). NMR (in $CDCl_3$) τ: 6.33 (1H, d, J=3.0 cps; 4βH), 7.18 (1H, d, J=3.0 cps; alcohol H), 9.32 (3H, 18–Me), 9.18, 9.08 (3H, 6H, side chain), 9.12 (3H, 19–Me).

3β-Methyl-2α,5α-ethanocholestane-3α,4α-diol (XXXII)——a) From XXXI: Compound (XXXI) (55 mg) was mixed with a CH_3MgI solution [prepared from Mg (37 mg) and MeI (0.080 ml) in anhydrous ether (5 ml)] and the mixture was refluxed for 1.5 hr, poured into ice–water, and extracted with ether. The residue obtained by the usual work-up was recrystallized from ether–MeOH and subsequently from ether–acetone to give XXXII (27 mg, 47%), mp 188—191°. A pure sample melts at 188—189°. *Anal.* Calcd. for $C_{30}H_{52}O_2$: C, 81.02; H, 11.79. Found: C, 80.61; H, 11.65. $[\alpha]_D^{24.5}$ +25.4±2° ($CHCl_3$, c=0.934). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3624, 3494, 1061.

b) From XXX: A mixture of the crude epoxy acetate (XXX) (319 mg), anhydrous benzene (5 ml), and a CH_3MgI solution [prepared from Mg (217 mg) and MeI (0.465 ml) in ahnydrous ether (10 ml) which thereafter was replaced with the same volume of anhydrous benzene] was refluxed for 15 hr. It was poured into 2 N HCl–ice and extracted with ether. The residue obtained by the usual work-up was chromatographed on neutral Al_2O_3 (9 g). Fractions eluted with benzene:$CHCl_3$ (4:1)–$CHCl_3$:MeOH (49:1) were recrystallized from ether–acetone to give XXXII (70 mg, 19%), mp 188—190°. For physical constants see a).

c) From V *via* 3-methyl-2α,5α-ethanocholest-3-ene (XXXIII): A solution of V (200 mg) in anhydrous ether (3 ml) was added dropwise to a CH_3MgI solution [prepared from Mg (146 mg) and MeI (0.31 ml) in in anhydrous ether (2 ml)], and the mixture was refluxed for 7 hr. It was poured into 2 N HCl–ice and extracted with ether. The IR spectrum of the reisude showed the presence of the carbonyl group, and therefore the residue was treated again with a freshly prepared CH_3MgI reagent [from Mg (146 mg) and MeI (0.31 ml) in anhydrous ether (2 ml)] in the same way described above. The usual work-up gave a crude sample of the methylhydrin, which was mixed with pyridine (1 ml) and $POCl_3$ (0.126 ml) with ice-cooling, and the mixture was kept stand overnight at room temperature. Ice was added to decompose an excess of $POCl_3$, and after 30 min, the mixture was poured into 2 N HCl–ice and extracted with ether:$CHCl_3$ (3:1). The usual work-up of the extract gave a residue which was proved to be a 5:6 mixture of XXXIII and XXXIV by gas liquid chromatography (GLC) on a QF-1 column (1.0%, 240°). The residue was recrystallized from ether–acetone to give crystals of mp 62.5—64° (a 5:6 mixture of XXXIII and XXXIV). A mixture of the crystals (100 mg), anhydrous benzene (10 ml) and *p*-toluenesulfonic acid (20 mg) was refluxed for 3 hr under nitrogen. It was diluted with 2 N Na_2CO_3 and extracted with ether. The residue (98 mg) obtained by the usual work-up was found to consist of a 3:1 mixture of XXXIII and XXXIV according to the GLC analysis.

To the mixture of the olefins (XXXIII) and (XXXIV) (97 mg) dissolved in anhydrous tetrahydrofuran (5 ml) was added dropwise with ice-cooling a solution of OsO_4 (61 mg) in anhydrous ether (1 ml), and the mixture was kept stand for 39 hr at room temperature. Into the reaction mixture diluted with tetrahydrofuran (12 ml) was introduced with ice-cooling H_2S-gas (washed with dil. $NaHCO_3$ solution) for 30 min, and the mixture was let stand for 30 min at room temperature. The precipitate was removed by filtration through a celite layer, and the filtrate was concentrated *in vacuo*, diluted with H_2O, and extracted with ether. The

ether layer was washed successively with 2 N HCl, H_2O, 2 N Na_2CO_3 and H_2C, dried, and evaporated. The residue (94 mg) was chromatographed on neutral Al_2O_3 (4 g). Fractions eluted with benzene:$CHCl_3$ (2:1)–$CHCl_3$ were recrystllized from ether–MeOH to give XXXII (34 mg, 28%), mp 184—188°. For physical data see a).

3-Methylene-2α,5α-ethanocholestane (XXXIII)——To 1.37 N ethereal solution of BuLi (2.5 ml) diluted with anhydrous ether (15 ml) was added methyltriphenylphosphonium bromide (1.72 g) with ice-cooling under nitrogen, and the suspension was stirred for 2 hr in a closed vessel. To the resulting yellow ylid solution was added dropwise V (613 mg) dissolved in anhydrous tetrahydrofuran (20 ml) and the ether was replaced by anhydrous tetrahydrofuran. The reaction was refluxed for 5 hr, poured into ice–water, and extracted with CH_2Cl_2. The residue (1.39 g) obtained by the usual work–up was chromatographed on neutral Al_2O_3 (22 g). Fractions eluted with petroleum ether were recrystallized from ether–acetone to give XXXIII (553 mg, 91%), mp 80—81.5°. A pure sample obtained by recrystallization from ether–MeOH melts at 82—83°. *Anal.* Calcd. for $C_{30}H_{50}$: C, 87.73; H, 12.27. Found: C, 88.21; 87.23; H, 12.32; 12.27. $[\alpha]_D^{25.5}$ +89.2±2° ($CHCl_3$, c=1.015). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3074, 1651, 877. NMR (in $CDCl_3$) τ: 5.26, 5.42 (AB type, 2H, olefinic H), 9.13 (3H, 19–Me).

3-Bromomethyl-2α,5α-ethanocholest-3-ene (XXXVI)——Compound (XXXIII) (165 mg) was dissolved in CCl_4 (35 ml), 10 ml of which was distilled to remove the moisture. N–Bromosuccimide (85.6 mg, 1.2 molar equiv.) and benzoylperoxide (4 mg) were added, and the mixture was refluxed for 3 hr under nitrogen. The mixture was concentrated, poured into ice–water, and extracted with $CHCl_3$. The residue [187 mg, no *exo*–methylene band (877 cm^{-1}) in its IR–spectrum] obtained by the usual work–up was recrystallized from CH_2Cl_2–MeOH to give XXXVI (140 mg, 71%), mp 111—119°. A pure sample melts at 117—120°. *Anal.* Calcd. for $C_{30}H_{49}Br$: C, 73.59; H, 10.08; Br, 16.32. Found: C, 73.28; H, 9.95; Br, 16.52. $[\alpha]_D^{26}$ +72.1 ±6° (acetone). NMR (crude sample, in CCl_4) τ: 6.01 (2H, allylic H), 415 (1H, olefinic H). Prolonged heating of the reaction mixture did not raise the yield.

3-Methylene-2α,5α-ethanocholestan-4α-ol (XXXVIII) *via* Epoxybromide (XXXVII)——A mixture of XXXVI (117 mg) anhydrous benzene (6.12 ml), and 0.332 M solution (1.08 ml, 1.5 molar equiv.) of perbenzoic acid in benzene was kept in the dark at room temperature for 61 hr. Analysis of an aliquot by the iodometry showed 97% consumption of the reagent. The reaction mixture was poured into a mixture of ice–water and 0.005 N $Na_2S_2O_3$ (45 ml) and extracted with ether. The ether layer was washed with 2 N NaOH, and H_2O, dried, and evaporated to give a crude sample of the epoxy bromide (XXXVII) (124 mg). This was mixed with Zn dust (1.24 g) and anhydrous EtOH (20 ml), and the suspension was refluxed with stirring for 4 hr. After removing Zn dust by decantation, the organic layer was evaporated *in vacuo*. The residue was extracted with ether, and the extract was washed with H_2O, dried, and evaporated. The residue was chromatographed on neutral Al_2O_3 (4 g). Fractions eluted with petroleum ether:benzene (4:1)—(2:1) were recrystallized from ether–MeOH to give XXXVIII (46.3 mg, 45%), mp 104.5—105.5°. A pure sample melts at 105—106°. *Anal.* Calcd. for $C_{30}H_{50}O$: C, 84.44; H, 11.81. Found: C, 84.29; H, 11.74. $[\alpha]_D^{26.5}$ +87.9±2° ($CHCl_3$, c=1.024). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3635, 3071, 1656, 1023, 902. NMR (in $CDCl_3$) τ: 5.01 (2H, olefinic H), 6.00 (1H, ether–H), 9.17 (3H, 19–Me). In another experiment, XXXVIII was obtained in 53% yield from XXXIII *via* crude XXXVI and XXXVII.

3-Methylene-2α,5α-ethanocholestane-4-one (XXXIX)——A mixture of XXXVIII (46.3 mg), pyridine (1 ml) and a pyridine–CrO_3 complex [prepared from CrO_3 (74 mg) and pyridine (1 ml)] was let stand for 13 hr at room temperature. The reaction mixture was poured into ice–water and extracted with ether. The ether layer was washed with 2 N H_2SO_4, H_2O, 2 N K_2CO_3, and H_2O, dried, and evaporated. The residue (45.6 mg) was recrystallized from ether–MeOH to give XXXIX (35.3 mg, 77%), mp 100—100.5°. A pure sample melts at 101—101.5°. *Anal.* Calcd. for $C_{30}H_{48}O$: C, 84.84; H, 11.39. Found: C, 85.13; H, 11.53. $[\alpha]_D^{25.5}$ +43.4±2° ($CHCl_3$, c=1.024). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3100, 1711, 1637, 941. UV λ_{max}^{EtOH} mμ (ε): 228 (5970), 339 (53). ORD: $[\phi]_{310\,m\mu}^{28}$ +3020, $[\phi]_{371\,m\mu}^{28}$ −700, $[\phi]_{379\,m\mu}^{28}$ −320, $[\phi]_{389\,m\mu}^{28}$ −670 (dioxane, c=0.295). NMR (in $CDCl_3$) τ: 4.07, 4.86 (2H, olefinic H).