The Effect of Methoxyl Groups on Carbonyl Infrared Absorption and on Optical Rotatory Dispersion. 2-Methoxy-3-keto- and 3-Methoxy-2-ketocholestanes[1]

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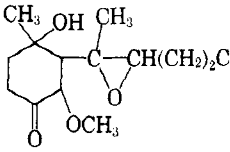
2α- and 2β-methoxy-3-ketocholestanes and 3α- and 3β-methoxy-2-ketocholestanes have been prepared from the corresponding alcohols. The alcohols were prepared by acid-catalyzed methanolysis from 2α,3α-epoxycholestane and 2β,3β-epoxycholestane, which were obtained by known routes. The equatorial methoxyl group in the ketones shifts the carbonyl absorption to higher frequency, but the axial methoxyl group causes no appreciable shift. The optical rotatory dispersion curves of these ketones show shifts similar to those observed with the corresponding acetoxy ketones.

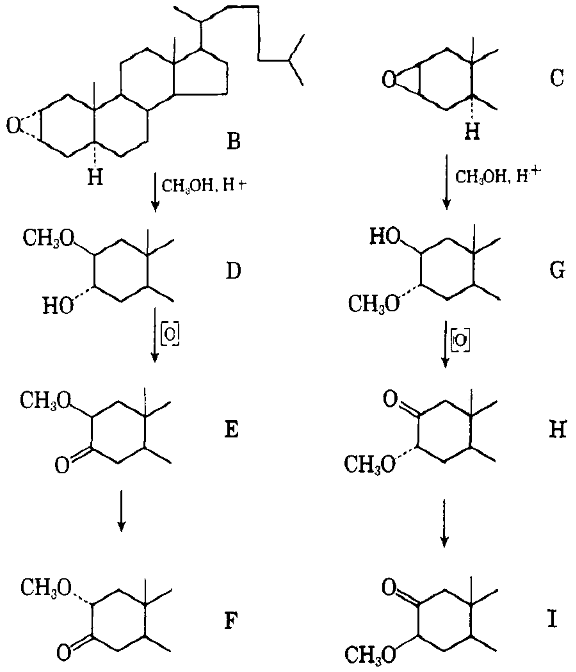
Structural elucidation of the antibiotic fumagillin[2] involved, as one key degradation product, a methoxy ketone which was assigned structure A, with the methoxyl group adjacent to the carbonyl group.[2] The carbonyl absorption of A was at a higher frequency (1724 cm.$^{-1}$) than is normal for cyclohexanones, and it was suggested that the methoxyl group was equatorial and that it, like an equatorial bromine atom, raised the carbonyl frequency. Since that time, the stereochemistry of the fumagillin series has been established by X-ray crystallography[3] and by chemical methods,[4] and it has been found that the methoxyl group is in fact equatorial.



A

The effect of equatorial halogen in raising the frequency of carbonyl absorption in the infrared is well-documented,[5] but at the time the present work was undertaken, there did not appear to be any data available about the effect of an equatorial or axial methoxyl group on the absorption of an adjacent carbonyl group. We have, therefore, prepared the axial and equatorial 2-methoxy-3-ketocholestanes, and the corresponding pair of 3-methoxy-2-ketocholestanes. It appears that, analogous to the bromo ketones, the equatorial methoxyl raises the carbonyl frequency, while the axial methoxyl group does not affect it appreciably. The optical rotatory dispersion (O.R.D.) curves for the four ketones have also been obtained.[6]

The methoxy ketones in the present work were prepared from 2α,3α-epoxycholestane (B), and from the corresponding 2β,3β-epoxy compound[7] C, by treatment with methanolic sulfuric acid, followed by oxidation.



The α-epoxide[8] B was obtained by peracid oxidation of Δ^2-cholestene. The latter was prepared by two methods: the dehydrohalogenation of 3β-chlorocholestane,[8,9] and the reduction of the 2α-bromo-3-hydroxycholestanes with zinc and acetic acid.[10] Treatment of the α-epoxide with methanol containing a trace of sulfuric acid or of *p*-toluenesulfonic acid gave 2-β methoxy-3α-hydroxycholestane (D), m.p. 159–160°, whose structure was assigned on the basis of the known[7,11] diaxial mode of ring opening of steroid epoxides. The structure D was also supported by the C–OH stretching frequency of 1012 cm.$^{-1}$, which is close to that found (996–1002 cm.$^{-1}$) for the axial hydroxyl in comparable compounds, as contrasted to that for equatorial hydroxyls (1037–1040 cm.$^{-1}$).[12]

In several runs, a compound (m.p. 149–150°), isomeric with D, was also obtained in the ring opening; the two products were separated by chromatography, but, in spite of some study, it was not possible to establish the structure of the second product. It

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[1] Supported in part by grant E-1138 of the U. S. Public Health Service.

[2] D. S. Tarbell, R. M. Carman, D. D. Chapman, K. R. Huffman, and N. J. McCorkindale, *J. Am. Chem. Soc.*, **82**, 1005 (1960); D. S. Tarbell, R. M. Carman, D. D. Chapman, S. E. Cremer, A. D. Cross, K. R. Huffman, M. Kunstmann, N. J. McCorkindale, J. G. McNally, Jr., A. Rosowsky, F. H. L. Varino, and R. L. West, *ibid.*, **83**, 3096 (1961).

[3] N. J. McCorkindale and J. G. Sime, *Proc. Chem. Soc.*, 331 (1961).

[4] J. R. Turner and D. S. Tarbell, *Proc. Natl. Acad. Sci. U. S.*, **48**, 733 (1962).

[5] (a) R. N. Jones, D. A. Ramsay, F. Herling, and K. Dobriner, *J. Am. Chem. Soc.*, **74**, 2828 (1952); (b) E. J. Corey, *ibid.*, **75**, 2301 (1953); E. J. Corey and H. J. Burke, *ibid.*, **77**, 5418 (1955); (c) C. Sandris and G. Ourisson, *Bull. soc. chim. France*, 958 (1956); (d) C. W. Shoppee and T. B. Bellas, *J. Chem. Soc.*, 3366 (1963).

[6] We are indebted to Professor Carl Djerassi of Stanford for the O.R.D. measurements.

[7] *Cf.* K. L. Williamson and W. S. Johnson, *J. Org. Chem.*, **26**, 4563 (1961).

[8] A. Furst and P. A. Plattner, *Helv. Chim. Acta*, **32**, 275 (1949).

[9] J. Mauthner, *Monatsh.*, **30**, 635 (1909).

[10] L. F. Fieser and X. A. Domínguez, *J. Am. Chem. Soc.*, **75**, 1704 (1953); G. H. Alt and D. H. R. Barton, *J. Chem. Soc.*, 4289 (1954).

[11] A. Furst and P. A. Plattner, Abstracts, XII International Congress of Pure and Applied Chemistry, 1951, p. 409; G. H. Alt and D. H. R. Barton, *J. Chem. Soc.*, 4284 (1954); R. E. Parker and N. S. Isaacs, *Chem. Rev.*, **59**, 781 (1959).

[12] A. R. H. Cole, R. N. Jones, and K. Dobriner, *J. Am. Chem. Soc.*, **74**, 5571 (1952).

TABLE I

CHARACTERISTIC INFRARED ABSORPTION OF CHOLESTANONES[a, b]

Ketones	Configuration[c] of $-OCH_3$	ν, cm.$^{-1}$ C=O	Δ C=O	C–OCH_3	Others
3-Ketocholestane		1718			
2β-Methoxy-3-ketocholestane (E)	ax	1719–1720 (s)	−1–+2	1082–1085 (s)	
2α-Methoxy-3-ketocholestane (F)	eq	1728–1729 (s)	+10–+11	1128	
3-Ketocholestane		1712			
3α-Methoxy-2-ketocholestane (H)	ax	1710–1717 (s)	−2–+5	1077 (s), 1084–1085 (sh), 1103–1101 (s)	1185 (w), 1198 (w), 1283 (w)
3β-Methoxy-2-ketocholestane (I)	eq	1720–1721 (s)	+8–+9	1120 (s), 1140 (s), 1150 (sh), 1137 (sh)	1193 (w), 1270–1278 (w, b)
2α-Bromo-3-ketocholestane	eq	1734–1735			

[a] The spectra were taken on 3–6 mg. of compound in 0.2–0.3 ml. of carbon tetrachloride; the values are given in cm.$^{-1}$. [b] b = broad, s = strong; w = weak; sh = shoulder. [c] ax = axial, eq = equatorial. [d] Taken in carbon disulfide [E. G. Cummins and J. E. Page, *J. Chem. Soc.*, 3847 (1957)].

could not be obtained in later runs, even after considerable variations in the conditions of ring opening. The oxidation of D to E and F was carried out using the chromic oxide–pyridine complex[13] or the chromic oxide–acetone–sulfuric acid reagent.[14] The axial methoxy ketone E was rapidly epimerized to F, and E was difficult to obtain analytically pure; in some runs, no attempt was made to isolate pure E, and the reaction mixture was epimerized directly to F by treatment with methanolic potash at room temperature. The stable equatorial methoxy ketone F was readily obtained pure, m.p. 127–128°.

2β,3β-Epoxycholestane (C), obtained by the action of base on 2α-bromo-3β-hydroxycholestane,[15] was converted to the 2-keto-3-methoxy compounds (H and I) by analogous procedures. Compound G showed a double m.p. 135–139° and 150–153°, which was not affected by chromatography or crystallization. Its precursors and the equatorial methoxy ketone I were obtained pure.

Infrared Absorption.—Table I shows that the equatorial methoxyl group does raise the carbonyl absorption frequency, but that the axial methoxyl group does not have a significant effect; there is thus a parallelism between the effect of the bromine[4] and the methoxyl, although the bromine has a larger effect.

The C–OCH_3 infrared frequency is also increased in the equatorial methoxy ketone, compared to the axial epimer. Thus, 2β-methoxy-3-ketocholestane (axial methoxyl) has the C–OCH_3 peaks in the 1085 cm.$^{-1}$ region, whereas in the 2α-methoxy-3-ketocholestane (equatorial methoxyl) the band is at 1128 cm.$^{-1}$, a shift of +43 cm.$^{-1}$. Similarly, 3α-methoxy-2-ketocholestane (axial) shows a doublet at 1079 and 1100 cm.$^{-1}$, which is shifted to 1120 and 1140 cm.$^{-1}$ in the equatorial compound. Page[16] reports a shift of +14 cm.$^{-1}$ in going from the axial to the equatorial isomer in 3α- and 3β-methoxycholestanes.

The results tabulated for the methoxy ketones E, F, H, and I are in agreement with several observations that have appeared while this work was in progress, showing that equatorial methoxyl groups increase the carbonyl frequency. Oxodihydroundulatine[17] shows carbonyl absorption at 1724 cm.$^{-1}$; epimerization, which presumably converts the axial methoxyl to the equatorial position, shifts the carbonyl band to 1730 cm.$^{-1}$. 2-Methoxy-*trans*-1-decalone (axial methoxyl) absorbs at 1715 cm.$^{-1}$, and the equatorial compound, obtained by epimerization, absorbs[18] at 1724 cm.$^{-1}$.

2α-Methoxy-3-keto-4,4-dimethylcholestane and the epimeric 2β-methoxy compound[19] were prepared by a displacement reaction of sodium methoxide on 2α-bromo-3-keto-4,4-dimethylcholestane; the 2β-methoxy compound absorbs at 1721 cm.$^{-1}$, and the 2α-methoxy compound at 1712 cm.$^{-1}$. The parent ketone, 4,4-dimethyl-3-ketocholestane, absorbs at 1692 cm.$^{-1}$. The increase in the carbonyl frequency of the 2β-methoxy compound, in which the methoxyl group should be axial, is attributed to the fact that this compound exists with ring A in the boat form, which puts the methoxyl group equatorial.[19] Similar relationships have been shown earlier for the 2α- and 2β-bromo-8-lanosten-3-ones.[20a]

It is possible, from the preceding observations, that the configurations assigned to the epimeric 16-methoxy-3β-hydroxy-17a,17a-dimethyl-D-homoandrostan-17-ones[20b] should be reversed. The observed carbonyl frequencies[20b] indicate this; the configurations were assigned on the assumption that an α-bromo ketone will be displaced by methoxide by a mechanism involving inversion, and this is an uncertain assumption at best. Both the carbonyl frequencies and C–OCH_3 stretching frequencies would fit better with reversed configurations at C-16 for the methoxyl groups.

Optical Rotatory Dispersion Values.—The observed values[6] for E, F, H, and I are given in Table II, along with the reported values for 2- and 3-ketocholestanes[21] and the values for the acetoxy analogs of E, F, H, and I.[22]

From Table II, it can be seen that an axial methoxyl group shifts the first extremun (peak) to longer wave

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[13] G. I. Poos, G. B. Arth, R. E. Beyler, and L. H. Sarett, *J. Am. Chem. Soc.*, **75**, 422 (1953).

[14] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946); R. G. Curtis, I. Heilbron, E. R. H. Jones, and G. F. Woods, *ibid.*, 457 (1953).

[15] E. J. Corey, *J. Am. Chem. Soc.*, **75**, 4832 (1953).

[16] J. B. Page, *J. Chem. Soc.*, 2017 (1955).

[17] E. W. Warnhoff and W. C. Wildman, *J. Am. Chem. Soc.*, **82**, 1472 (1960).

[18] H. O. House and H. Thompson, *J. Org. Chem.*, **28**, 165 (1963).

[19] H. P. Sigg and C. Tamm, *Helv. Chim. Acta*, **43**, 1402 (1960).

[20] (a) D. H. R. Barton, D. A. Lewis, and J. F. McGhie, *J. Chem. Soc.*, 2907 (1957); (b) M. Uskokovic, M. Gut, and R. Dorfman, *J. Am. Chem. Soc.*, **82**, 958 (1960).

[21] (a) C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 42; (b) C. Djerassi, W. Closson, and A. E. Lippman, *J. Am. Chem. Soc.*, **78**, 3163 (1956).

[22] K. L. Williamson and W. S. Johnson, *ibid.*, **83**, 4623 (1961).

TABLE II

OPTICAL ROTATORY DISPERSION VALUES OF STEROIDAL METHOXY KETONES AND RELATED COMPOUNDS

Compound	Peak, mμ	$\Delta\lambda_{ax}$[a]	$\Delta\lambda_{eq}$[a]	a × 10^{-2}[b]
2-Ketocholestane	310			
3α-Methoxy-2-ketocholestane (H)	327	+17		+18.8
3β-Methoxy-2-ketocholestane (I)	314		+4	+23.8
3-Ketocholestane	307			
2β-Methoxy-3-ketocholestane (E)	310	+3		+5.09
2α-Methoxy-3-ketocholestane (F)	304		−3	+12.8
3α-Acetoxy-2-ketocholestane[c]	317	+7		+11.7
3β-Acetoxy-2-ketocholestane[c]	305		−5	+27.2
2β-Acetoxy-3-ketocholestane[c]	290	−17		+2.7
2α-Acetoxy-3-ketocholestane[c]	305		−2	+14.1

[a] $\Delta\lambda_{ax}$ and $\Delta\lambda_{eq}$ are the shifts from the parent ketone of the axial and equatorial methoxy ketones. [b] a = amplitude; this is the amplitude when [α] × 10^{-2} is plotted against λ; the values for the acetoxy ketones and the unsubstituted ketocholestanes were taken from the published[21,22] curves. [c] These values were taken from ref. 22.

lengths, whereas an equatorial group has a smaller effect, shifting the wave length slightly higher in one case and slightly lower in the other case. This is similar to the 12-acetoxy-11-keto steroids[23] where the axial acetoxy group shifts the wave length +15 mμ, while the equatorial substituent shifts the wave length −7 and −2.5 mμ. The shift in the 3α- and 3β-methoxy ketones is also similar to the corresponding 3α- and 3β-acetoxy ketones in Table II.

There is, however, a considerable difference in the shift associated with the 2β-methoxy-3-ketocholestane and that associated with the 2β-acetoxy-3-ketocholestane. Williamson and Johnson[22] consider the unusual effect of the 2β-acetoxy group as evidence for a distortion of ring A from the normal chair form to a twist conformation. Their n.m.r. data also indicate this distortion.

It is interesting to note that the amplitudes of the dispersion curves of the equatorial methoxy ketones are higher than those of the axial compounds. This is in direct contrast to 12-acetoxy-11-keto steroids, which show an increase in amplitude for the axial substituent compared with its equatorial epimer.[24]

Experimental[25]

Δ^2-Cholestene, prepared from 3β-chlorocholestane and quinoline,[8,9] was purified in two ways: by chromatography on alumina or by conversion to the dibromide, followed by debromation. The material from the dibromide melted at 73–74°; the chromatographic purification gave material of m.p. 71°, $[\alpha]^{27}\text{D}$ +70.1°; lit.[10,25] m.p. 74–75°, [α]D +66°.

Δ^2-Cholestene from the zinc–acetic acid reduction of the 2α-bromo-3-hydroxycholestanes[10] melted at 75°, after chromatography and crystallization from ether–methanol.

2α,3α-Epoxycholestane (B) was prepared from Δ^2-cholestene and standardized monoperthalic acid[27] in 72% yield, after recrystallization from ether–methanol; it showed m.p. 103–105°, $[\alpha]^{28}\text{D}$ +35.1°. Furst and Plattner[8] reported the properties as m.p. 105–106°, [α]D +36.0°.

2β-Methoxy-3α-hydroxycholestane (D). A.—To a stirred solution of 2α,3α-epoxycholestane (B, 4.61 g.) dissolved in anhydrous methanol (750 ml.) was added one drop of concentrated sulfuric acid. After 15 hr. of continuous stirring, barium carbonate was added, and the mixture was filtered. Evaporation to near dryness produced a white crystalline compound. Recrystallization from ether–methanol gave 4.39 g. (88%) of an alcohol mixture, m.p. range 130–150°. The infrared spectrum of this mixture showed characteristic peaks at 1012 (C–OH), 1031 (C–OH), and 1089 cm.$^{-1}$ (broad, C–OCH_3).

Anal. Calcd. for $C_{28}H_{50}O_2$: C, 80.32; H, 12.04. Found: C, 80.31; H, 11.76.

Two alcohols could be separated from this mixture by repeated chromatography (both eluted with 19:1 benzene–ethyl acetate). The lower melting unknown compound X (m.p. 149–150°) was eluted first, and showed characteristic infrared peaks at 1031 (C–OH) and 1089 cm.$^{-1}$ (broad, –OCH_3); $[\alpha]^{26}\text{D}$ +35.1 ± 7° (*c* 1.270).

Anal. Calcd. for $C_{28}H_{50}O_2$: C, 80.32; H, 12.04. Found: C, 80.58; H, 11.81.

The second compound, **2β-methoxy-3α-hydroxycholestane** (**D**), m.p. 159–160°, showed characteristic infrared peaks at 1031 (shoulder), 1012 (C–OH), and 1089 cm.$^{-1}$ (broad, C–OCH_3); [α]D +28.6 ± 3.2 (*c* 2.155), +22.6 ± 5.2° (*c* 1.520).

Anal. Calcd. for $C_{28}H_{50}O_2$: C, 80.32; H, 12.04. Found: C, 80.17; H, 12.11.

B.—2α,3α-Epoxycholestane (0.111 g.) was dissolved in anhydrous methanol (100 ml.), and to this solution were added a few crystals of *p*-toluenesulfonic acid. The resulting solution was stirred for 3.5 hr. in a dry nitrogen atmosphere. The catalyst was neutralized with sodium carbonate, and the crude product was obtained as in procedure A in almost quantitative yield. The infrared spectrum of the crude material showed C–OH absorption mostly at 1012 cm.$^{-1}$ and the presence of unchanged epoxide. A single chromatography gave the pure alcohol D, m.p. 158–160°.

In a dry nitrogen atmosphere, catalysis with a trace of concentrated sulfuric acid gave results analogous to those with *p*-toluenesulfonic acid as catalyst.

The two alcohols gave a markedly depressed mixture melting point. Attempts to prepare quantities of unknown X by procedure A were unsuccessful, for the reaction proved to be inconsistent. In later runs, no X was observed, and, as in procedure B, one chromatography gave D, m.p. 159–160°, exclusively.

2β-Methoxy-3-ketocholestane (E). A.—Chromic acid–pyridine complex[12] (0.25 g. in 1 ml.) was added to 2β-methoxy-3α-hydroxycholestane (D), 0.208 g.) dissolved in pyridine (3 ml.). This mixture was left at room temperature for 27 hr., after which time it was poured into water (80 ml.). The aqueous solution was extracted four times with ether (50-ml. portions) and the ether layer was then washed three times with water (50-ml. portions) and once with a very dilute solution of hydrochloric acid. The ether solution was dried, filtered, and concentrated. Dilution with methanol gave a 50% yield of a solid which, when recrystallized from ether–methanol, had m.p. 77–80°. The infrared spectrum of this compound showed characteristic peaks at 1082–1085 (C–OCH_3) and at 1719–1720 cm.$^{-1}$ (C=O).[28] In other runs, the sharp carbonyl absorption of the 2β-methoxycholestan-3-one ranged from a low of 1716 cm.$^{-1}$ to a high of 1721 cm.$^{-1}$.

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[23] Ref. 21a, p. 114.

[24] W. Klyne, "Advances in Organic Chemistry," Vol. 1, R. A. Raphael, Ed., Interscience Publishers, Inc., New York, N. Y., 1960, p. 292. We are indebted to Professor Klyne for informing us of this reference.

[25] All melting points are uncorrected. Microanalyses are by Mr. V. Landeryou and Mr. A. Revilla in this laboratory, and by Micro-Tech Laboratories, Skokie, Ill. Infrared spectra obtained on Perkin-Elmer Models 21 and 421 spectrophotometers. All infrared spectra were taken in carbon tetrachloride unless otherwise indicated. All optical rotations are at room temperature in chloroform. Chromatography was carried out on neutral activity grade I Woelm alumina unless otherwise indicated. The O.R.D. curves for the four methoxy ketones described in this paper are given in the Ph.D. thesis of S. S. Stradling, University of Rochester, 1963.

[26] D. H. R. Barton and W. J. Rosenfelder, *J. Chem. Soc.*, 2459 (1949); 1048 (1951).

[27] E. E. Royals and L. L. Harrell, Jr., *J. Am. Chem. Soc.*, **77**, 3405 (1955).

[28] The λ_{max} values listed for this and subsequent ketones were taken directly from the machine at very slow scanning times; for the other spectra, the values were taken from the paper.

B.—To a stirred solution of 2β-methoxy-3α-hydroxycholestane (0.027 g.) in acetone (3 ml.) at room temperature was added one drop of 8 *N* chromic acid–sulfuric acid solution.[14] This solution was stirred for 2 min. and was quenched with 2 ml. of 10% aqueous sodium bicarbonate. It was poured into a 3:1 water–ether mixture and, after shaking, the ether was poured through anhydrous sodium sulfate. Crystallization from ether–methanol yielded 2β-methoxy-3-ketocholestane. Recrystallization from this solvent mixture gave a 40% yield of a compound melting 75–76.5°. Further recrystallization raised the melting point to 77.5–79°. The infrared spectrum showed absorption at 1080–1083 (C–OCH_3) and 1716 cm.$^{-1}$ (C=O).

The 2β-methoxyl group appears to be very labile[7] and, consequently, contact with acidic or basic substances causes some epimerization. Attempts to separate pure 2β-methoxy-3-ketocholestane by column chromatography on neutral alumina (either activity grade I or III) or on silica gel caused partial epimerization, and though the ketones could be separated from unchanged alcohol and other oxidation products, they could not be separated from each other.

The infrared spectrum of the ketone obtained by either procedure A or procedure B indicates nearly absolute configurational purity of the methoxyl group and very little, if any, unchanged alcohol.

The rotatory dispersion curve in methanol (*c* 0.052) shows $[\alpha]_{600}$ +96, $[\alpha]_{589}$ +106, $[\alpha]_{310}$ +576, $[\alpha]_{265}$ +67.2, and $[\alpha]_{250}$ +163°.

2α-Methoxy-3-ketocholestane (F).—To a stirred solution of 2β-methoxy-3α-hydroxycholestane (D, 0.240 g.) in acetone (35 ml.) at 5° was added dropwise an 8 *N* solution of chromic acid–sulfuric acid[14] until a permanent orange-brown color was imparted to the solution. After 10 min., the solution was poured into water and the water solution was extracted with ether (60 ml.). The ether layer was washed with water and dried with anhydrous magnesium sulfate. The drying agent was filtered, and the solvent was evaporated under reduced pressure to give an oil. This oil was crystallized from an ether–methanol mixture, to yield 0.166 g. of a mixture of the two epimeric ketones (2β-methoxy- and 2α-methoxy-3-ketocholestane) along with other products.

The product mixture was dissolved in 25 ml. of a 4% solution of potassium hydroxide in methanol, was stirred for 3 hr. in a nitrogen atmosphere, and was neutralized with dilute aqueous hydrochloric acid. The resulting solution was extracted twice with ether (40-ml. portions), and the ether solution was dried. Concentration of the ether solution with subsequent dilution with methanol gave 0.142 g. of product mixture. The crude ketonic product was chromatographed on 4.2 g. of neutral alumina and 40 mg. of the pure product was eluted with 49:1 benzene–ethyl acetate. Recrystallization from ether–methanol gave 2α-methoxy-3-ketocholestane (F), m.p. 127–128°. The ketone showed infrared absorption at 1728–1729 (C=O) and 1128 cm.$^{-1}$ (C–OCH_3). In some other samples, the carbonyl peak was observed as low as 1726 cm.$^{-1}$.

Anal. Calcd. for $C_{28}H_{48}O_2$: C, 80.71; H, 11.61. Found: C, 80.89; H, 11.51.

The rotatory dispersion curve in methanol (*c* 0.108) shows $[\alpha]_{598}$ +18.5, $[\alpha]_{589}$ +18.5, $[\alpha]_{304}$ +850, $[\alpha]_{264-260}$ −426, and $[\alpha]_{240}$ −222°.

2β,3β-Epoxycholestane (C) was prepared in 80% yield by Corey's procedure,[15] and had the properties, m.p. 89–90°, $[\alpha]_D$ +50.1°. Furst and Plattner[8] report for this compound m.p. 87.5–88.5°, $[\alpha]_D$ +50.5° (*c* 1.492), while Corey[15] reports m.p. 89–90°, $[\alpha]^{25}_D$ +57.4 ± 1.0° (*c* 1.53). The infrared spectrum of this compound shows characteristic absorption at 1255, 1080–1085, and 1005–1020 cm.$^{-1}$.

3α-Methoxy-2β-hydroxycholestane (G).—The same procedures were used for the preparation of G that were employed for the preparation of 2β-methoxy-3-ketocholestane (E).

Recrystallization of the crude material from ether–methanol gave a compound which exhibited a double melting point, m.p. 135–139° and m.p. 150–153°. Chromatography on neutral alumina and recrystallization from acetone gave unchanged material. The infrared spectrum showed characteristic peaks at 3623 (C–OH), 1087 (C–OCH_3), and 1016 cm.$^{-1}$ (broad, C–OH); $[\alpha]^{27}_D$ +41.1 ± 5.6°.

Anal. Calcd. for $C_{28}H_{50}O_2$: C, 80.32; H, 12.04. Found: C, 80.22; H, 11.75.

3α-Methoxy-2-ketocholestane (H). A.—3α-Methoxy-2β-hydroxycholestane was oxidized with chromic acid–pyridine complex as described previously for the preparation of the isomeric ketone E. Recrystallization of the material obtained by this procedure from either ether–methanol or ether–ethanol gave silky needles in 51% yield, m.p. 125–127°.

B.—3α-Methoxy-2β-hydroxycholestane was also oxidized with chromic acid–sulfuric acid as described previously for the preparation of E. Recrystallization of the ketone obtained from ether–methanol gave silky needles in 76% yield, m.p. 125–127°.

The infrared spectra of the ketones obtained by these two procedures were identical and showed characteristic absorption at 1713–1710 (C=O), 1100, and 1079 cm.$^{-1}$.

Anal. Calcd. for $C_{28}H_{48}O_2$: C, 80.71; H, 11.61. Found: C, 80.00; H, 11.55; residue, 1.02.

The analysis, as indicated, showed that this material was slightly impure and contained a noncombustible residue. This residue may be due to some type of chromium compound from the oxidation which is not removed by recrystallization. No chromatographic separation was attempted for fear that some epimerization of the methoxyl group might occur.

The rotatory dispersion curve in methanol (*c* 3.84 mg./2 ml.) shows $[\alpha]_{589}$ +60, $[\alpha]_{327}$ +1100, and $[\alpha]_{285}$ −780°.

3β-Methoxy-2-ketocholestane (I).—The epimerization of the 3α-methoxy ketone H to the 3β-methoxy ketone I was carred out with potassium methoxide as described previously for the conversion of E to F. The compound obtained was recrystallized from ether–methanol to give pure material, m.p. 106.5–108°. The infrared absorption was at 1720–1721 (C=O), 1140, and 1120 cm.$^{-1}$ (C–OCH_3).

Anal. Calcd. for $C_{28}H_{48}O_2$: C, 80.71; H, 11.61. Found: C, 81.00; H, 11.62.

The rotatory dispersion curve in methanol (*c* 3.64 mg./2 ml.) shows $[\alpha]_{589}$ +90, $[\alpha]_{414}$ +1400, and $[\alpha]_{276}$ −980°.