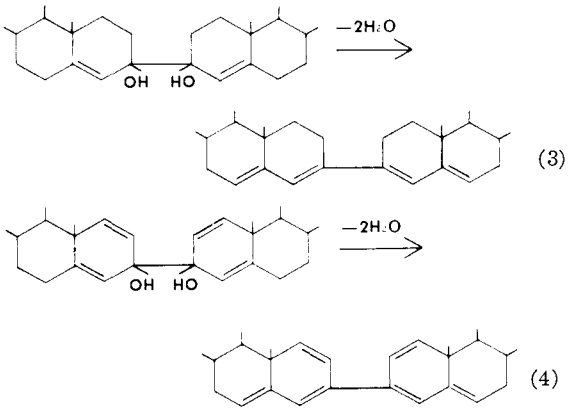
This product should give a second wave corresponding to the reduction of the Δ^4-3-ketosteroid or the Δ^1-3-ketosteroid depending on the coupling points. No such wave is in evidence. The pinacol formation product, reaction 2, contains no conjugation and therefore should be polarographically inert in the range studied. Reaction 2 then probably corresponds to the electrode process in acid solution and probably accounts for the major part of the electrode reaction in the alkaline solutions for at least three of the compounds investigated.

The electrode process involved in the reduction of prednisone in alkaline solutions is apparently somewhat different from that of the other three compounds. The height and *p*H dependency of the first wave indicate that the corresponding electrode reaction is a one-electron, reversible process. The height and *p*H-independent nature of the second wave (varies only 0.06 volt over a *p*H span of 4.5 units) indicate that it is probably a one-electron, irreversible process. The total electrode process at some point on the diffusion plateau of the second wave would then correspond to a one-electron reversible step, followed closely by a one-electron irreversible step. This is essentially the same process proposed by Coulson and Crowell[13] for the reduction of benzaldehyde at the dropping mercury electrode.

Controlled Potential Electrolysis.—Macro amounts of prednisone, cortisone, prednisolone and hydrocortisone in 50% ethanol solutions having a *p*H of 5.5 have been electrolyzed at a stirred mercury pool cathode at controlled potentials. A low threshold current integrator has given *n*-values between 0.9 and 1.0 electron per molecule for the reduction of each of these compounds. The isolated electrolysis products which have not been completely characterized no longer have the Δ^4-3-keto or $\Delta^{1,4}$-3-keto ultraviolet absorption. Upon dehydration, the cortisone and the hydrocortisone reduction products yielded compounds having ultraviolet absorption maxima at 294, 308 and 323 mμ in methanol. These values agree well with the absorption maxima reported[14] for the tetraene structure in 3,3′-bis-3,5-cholestadiene. Upon dehydration, the prednisone and the prednisolone reduction products yielded compounds having a single absorption maximum at 316 mμ rather than the triplet listed above.



These preliminary studies seem to substantiate the hypothesis that the one-electron reduction product of these steroids is a pinacol.

(13) D. M. Coulson and W. R. Crowell, THIS JOURNAL, **74**, 1290 (1952).

(14) R. Dulou, J. Chopin and Y. Raoul, *Bull. soc. chim. France*, 616 (1951).

BLOOMFIELD, NEW JERSEY

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Spectral and Stereochemical Studies with Deuterated Cyclohexanes[1]

BY E. J. COREY, M. GERTRUDE HOWELL, ALMA BOSTON, RICHARD L. YOUNG AND RICHARD A. SNEEN

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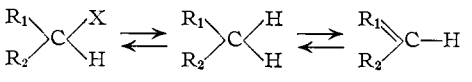
Analysis of infrared absorption due to C–D stretching vibrations is introduced as a tool for determining the orientation of deuterium substituents in cyclohexane systems. The utility of the method is shown by its applicability in three varied examples to distinguish between epimers having axial and equatorial deuterium. The stereochemistry of the reduction of cholesteryl tosylate with lithium aluminum hydride has been studied with deuterium tracer with the finding that the reaction proceeds by way of the cyclocholesteryl cation (substitution at C_3 with retention of configuration) instead of by concerted nucleophilic displacement. The stereochemistry of electrophilic substitution by hydrogen also has been studied briefly and has been found to involve retention of configuration to a high degree in the cases studied.

Stereochemistry is a matter of interest whenever carbon–hydrogen bonds are formed or broken in the system II ⇄ I ⇄ III.



II I III

In each step the acquisition or loss of hydrogen may take place in either of two ways which differ stereochemically because they involve a different spatial relationship between the leaving or entering hydrogen, the central carbon atom and the remaining substituents. The stereochemistry of these transformations is usually studied by the substitution of deuterium or tritium in place of one of the hydrogens of I because of the fact that with singly and stereospecifically labeled I the stereochemistry of the change II ⇄ I ⇄ III can be determined by methods which take advantage of the isotope-induced asymmetry in I. When operable, these methods are capable of distinguishing between the two stereoisomeric forms of labeled I having opposite configurations at the central carbon atom.

(1) Taken in part from the B.S. Theses of M. H., A. B. and R. L. Y.

In principle these stereoisomeric forms of labeled I are distinguishable by means of optical rotation; in practice, however, this technique leaves much to be desired because the rotational differences between the isomers may be very small. In the case of deuterium labeled compounds of type I in which the deuterated carbon atom is the *only* asymmetric center a difference in optical rotation between the pure antipodes of the order of 1° may be expected.[2] Such a difference is large enough to be of value in stereochemical studies if rotations are measured with precision.[3] In the case of deuterium labeled compounds of type I in which there are other additional asymmetric centers, however, the use of optical rotation becomes impractical because of the difficulty of completely freeing the substance being studied from the optically active impurities which are invariably produced or which remain as contaminants during synthetic operations.

Stereospecific interaction with an asymmetric substance such as an enzyme provides another method for distinguishing between stereoisomeric forms of labeled I. This technique, which has been used with 1-deuteroethanol,[4] is of limited applicability because of its restricted scope.

In the cases where the groups R_1 and/or R_2 of singly labeled I contain asymmetric centers there also exists the possibility of differentiating between stereoisomers by means of spectroscopic studies since the stereoisomers are diastereomeric. In particular, the special case of isomeric deuterium labeled compounds of type I in which hydrogen and deuterium are attached to a six-membered ring seemed especially favorable for such an approach since the deuterium atom possesses different orientations, axial and equatorial, in the two isomers to be distinguished. Furthermore, we were especially interested in the properties of deuterated cyclohexanes in connection with stereochemical and biostereochemical studies. This paper describes the stereospecific synthesis of a number of deuterated cyclohexane systems and the applicability of infrared spectroscopy in determining orientation of deuterium[5] and certain points of stereochemistry.

Three sets of epimeric deuterated compounds were synthesized and were subjected to careful infrared absorption analysis. Examination of the absorption due to C–D stretching vibrations in each of these cases permitted clear differentiation between the epimers of each set and this absorption was characteristic enough to be used for identification.

3β-Deuterocholestane (equatorial deuterium) was synthesized by the sequence cholestanone → 3α-deuterocholestan-3β-ol (by lithium aluminum deuteride reduction) → 3α-deuterocholestan-3β-ol tosylate → 3β-deuterocholestane (by lithium aluminum hydride reduction). The isomeric 3α-deuterocholestane was synthesized by reduction of cholestan-3β-ol tosylate with lithium aluminum deuteride. The 3β-deutero isomer showed *two* absorption bands in the C–D stretching region at 2155 cm.$^{-1}$ (strong) and 2177 cm.$^{-1}$ (medium) and, in contrast, the 3α-deutero isomer showed a displaced doublet at 2129 cm.$^{-1}$ (medium) and 2154 cm.$^{-1}$ (strong) (Fig. 1). The 2154–55 cm.$^{-1}$ band is common to both and is the stronger band in the doublet. The 2177 and 2129 bands, however, are unique to the β- and α-isomers, respectively, and allow easy differentiation. 3,3-Dideuterocholestane, on the other hand, showed two strong sharp bands at 2104 and 2187 cm.$^{-1}$, *i.e.*, above the highest and below the lowest observed frequencies for the 3-monodeuterocholestanes, together with weak absorption at *ca.* 2155 cm.$^{-1}$, which may be due to contamination by 3-monodeuterocholestanes, and a very slight shoulder at *ca.* 2087 cm.$^{-1}$.[6]

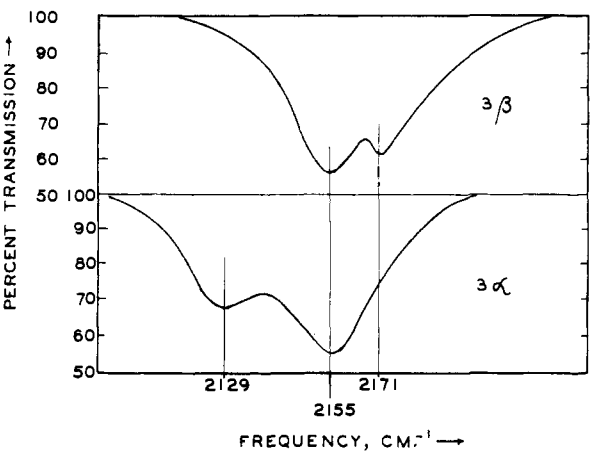


Fig. 1.—Infrared absorption in the C–D stretching region: upper curve, 3β-deuterocholestane; lower curve, 3α-deuterocholestane.

trans-1-Deutero-4-phenylcyclohexane was synthesized by the sequence 4-phenylcyclohexanone → 1-deutero-*trans*-4-phenylcyclohexanol (lithium aluminum deuteride reduction) → 1-deutero-*trans*-4-phenylcyclohexyl tosylate → *trans*-1-deutero-4-phenylcyclohexane. *cis*-1-Deutero-4-phenylcyclohexane was synthesized by the reduction of *trans*-4-phenylcyclohexyl tosylate with lithium aluminum deuteride. The infrared spectrum of *trans*-1-deutero-4-phenylcyclohexane (equatorial deuterium) showed C–D stretching absorption at 2171 cm.$^{-1}$ [7] whereas the spectrum of the *cis* isomer (axial deuterium) showed absorption at 2158 cm.$^{-1}$.[7] Consequently the axial and equatorial orientations

(2) See E. Eliel, THIS JOURNAL, **71**, 3970 (1949).

(3) For such studies on 1-deutero-butan-1-ol, see A. Streitwieser, *ibid.*, **77**, 1117 (1955).

(4) F. A. Loewus, F. H. Westheimer and B. Vennesland, *ibid.*, **75**, 5018 (1953).

(5) For a preliminary account of this work see E. J. Corey, R. A. Sneen, M. G. Danaher, R. L. Young and R. L. Rutledge, *Chemistry and Industry*, 1294 (1954).

(6) The lack of correspondence between the C–D stretching absorption of 3,3-dideuterocholestane and the summation of the C–D stretching absorptions of 3α- and 3β-monodeuterocholestanes can be attributed to vibrational interactions in the dideutero compound with the occurrence of symmetric and antisymmetric vibrations. An analogous vibrational interaction is apparent in the case of dideuteromethane, ν_{max} 2139, 2255 cm.$^{-1}$ as compared to ν_{max} 2204 cm.$^{-1}$ for monodeuteromethane; G. Herzberg, "Infrared and Raman Spectra of Polyatomic Molecules," D. Van Nostrand Co., Inc., New York, N. Y., 1945, p. 309.

(7) A very slight absorption, possibly due to contamination by an isomeric substance, occurs at 2119 cm.$^{-1}$ Deuterium is not incorporated into phenylcyclohexane with lithium aluminum deuteride under the conditions used for the above deuteride reductions. These absorption data indicate that the less stable chair conformation having phenyl axial cannot be present to the extent of more than a few per cent.

of deuterium are easily distinguished in the case of a simple monocyclic cyclohexane derivative as well as in the case of the more complex steroids.

The data on the 1-deutero-4-phenylcyclohexanes allows positive assignment of the two C–D stretching bands observed by Larnaudie[8] in the spectrum of deuterocyclohexane at 2174 and 2146 cm.$^{-1}$ to the chair forms with deuterium equatorial and axial, respectively, identical with Larnaudie's original assignment.

The spectrum of 1,1-dideutero-4-phenylcyclohexane showed complex C–D stretching absorption consisting of four bands at 2201, 2189, 2160 and 2106 cm.$^{-1}$, again indicating that C–D vibrational interaction can be expected with *gem*-deuterium substituents.

6α- and 6β-deutero-3β-acetoxycholestan-7-one were prepared by methods to be described elsewhere and were found to exhibit absorption at 2137(s), 2181(m) cm.$^{-1}$ and 2134(m) and 2164(s) cm.$^{-1}$, respectively. In this case the spectral difference between epimers is not as great as with the 3-deuterocholestanes, but still large enough to allow clear differentiation. 6,6-Dideutero-3β-acetoxycholestan-7-one, as expected, showed absorption characteristic of perturbed C–D stretching vibrations at 2131 and 2220 cm.$^{-1}$.

In each of the three sets of epimers described above the high-frequency absorption band of the isomer with equatorial deuterium occurs at a higher frequency than the high-frequency band of the corresponding axial isomer. A limited study of the spectra of some chlorinated cyclohexane systems indicates a parallel trend in axial and equatorial C–Cl stretching frequencies.[5] 3β-Chlorocholestane and 3β-chloro-Δ^5-cholestene (equatorial chlorine) exhibit C–Cl stretching absorption at 758 and 760 cm.$^{-1}$, respectively, whereas 3α-chlorocholestane (axial chlorine) exhibits two bands in the C–Cl stretching region at 708 and 737 cm.$^{-1}$, both of lower frequency than is observed with the 3β-chloro compounds. A further similarity to the deuterated cyclohexanes is apparent in the C–O stretching absorption of 3-hydroxysteroids, the frequency of which depends on the orientation of the hydroxyl function and is usually greater for the equatorial than for the axial arrangement.[9]

The occurrence of two absorption bands due to C–D stretching vibrations is a highly interesting feature in the spectra of most of the monodeuterosteroids, which for the time being must remain unexplained. Although this separation of C–D stretching absorption into doublet bands cannot be anticipated for a specific case and is a complicating factor, it does not seem to nullify the application of the infrared method to distinguishing between epimers. Further studies of this effect are underway to try to determine whether it is due to the presence of more than one rotational form or whether it arises from a single molecular species because of vibrational interaction. In this connection it is of interest to note that 3α-deuterocholestan-3β-ol tosylate exhibits no less than five distinct C–D stretching bands (2101, 2146, 2166, 2192 and 2206 cm.$^{-1}$) and that 3α-deuterocholestan-3β-ol shows no less than three bands (*ca.* 2090, 2117, 2143 cm.$^{-1}$). In these cases it seems likely that the multiplicity of C–D stretching bands arises in part because of the presence of more than one rotational isomer.

Further data on the infrared absorption of deuterated steroids is given in Table I including the spectra of several α-deuteroketones. The absorption of 6β-deuterocholestan-3β,7α-diol-3-acetate (2133, 2156 cm.$^{-1}$) is quite similar to that of the corresponding 7-ketone (2134, 2164 cm.$^{-1}$). A somewhat greater difference exists between 2β-deuterocholestan-3α-ol and the corresponding 3-ketone, however, indicating that C–D stretching absorption can be expected to vary with changing substitution on an adjacent atom. The spectra of the 5α- and 7α-deuterated 6-ketones are especially interesting because these substances show but a single C–D stretching band. While it is possible that this band is a composite of two equally intense bands which are too close together to be resolved, it nonetheless seems to be of possible significance that the C–D group of these 5α- and 7α-deuterated 6-ketones ought to be less affected by the rotational position of the angular methyl group at C_{10} than those of the other deuterated substances reported herein.

TABLE I

Compound	C–D stretching absorption (cm.$^{-1}$)	
6β-Deuterocholestan-3β,7α-diol monoacetate	2133	2156
2β-Deuterocholestan-3α-ol	2161	2171[a]
2β-Deuterocholestan-3-one	2145	2153[b]
5α-Deutero-3β-acetoxy-cholestan-6-one	2125	
7α-Deutero-3β-acetoxy-cholestan-6-one	2138	

[a] Shoulder. [b] Shoulder, not well resolved.

The above data on 3-deuterated steroids make it possible to determine the stereochemical course of a number of reactions of the type II $\rightleftarrows$ I $\rightleftarrows$ III and, consequently, provide information as to mechanism. The reduction of cholesteryl tosylate by lithium aluminum hydride, which affords a mixture of Δ^5-cholestene and 3,5-cyclocholestane,[10] is a good example. Although displacement reactions of cholesteryl tosylate in polar media, *e.g.*, alcohol, acetic acid, proceed *via* the cyclocholesteryl cation[11] and invariably lead to the β-orientation of the substituent at C_3, such a pathway need not obtain in weakly or non-polar media which ought to favor direct displacement, especially with a highly nucleophilic reagent. Thus, although Δ^5-cholestene and 3,5 cyclocholestane might be formed by reaction of 3,5-cyclocholesteryl cation with aluminum hydride ion, they might also be formed directly from cholesteryl tosylate by direct attack by aluminum hydride at C_3 and C_6, respectively. If the former possibility obtains, the unsaturated reduction

(8) M. Larnaudie, *Compt. rend.*, **235**, 154 (1952).

(9) (a) A. R. Cole, R. N. Jones and K. Dobriner, THIS JOURNAL, **74**, 5571 (1952); A. Furst, H. H. Kuhn, R. Scotoni and H. H. Gunthard, *Helv. Chim. Acta*, **35**, 951 (1952); (b) for recent studies on halides see D. H. R. Barton, J. E. Page and C. W. Shoppee, *J. Chem. Soc.*, 331 (1956).

(10) H. Schmid and P. Karrer, *Helv. Chim. Acta.*, **32**, 1371 (1949).

(11) S. Winstein and R. Adams, *ibid.*, **70**, 838 (1948).

product formed with lithium aluminum deuteride should be 3β-deutero-Δ⁵-cholestene, whereas the latter possibility requires it to be 3α-deutero-Δ⁵-cholestene. The point was settled by conversion of cholesteryl tosylate with lithium aluminum deuteride to a 3-deutero-Δ⁵-cholestene which was identified as the 3β-deutero epimer by catalytic reduction to 3β-deuterocholestane, identical in the infrared with an authentic sample prepared as described above. The reaction of cholesteryl tosylate with lithium aluminum hydride in ether, therefore, does appear to proceed *via* the cyclocholesteryl cation instead of by direct displacement.

The 6-deutero-3,5-cyclocholestane produced by the reaction of cholesteryl tosylate with lithium aluminum deuteride manifested C–D stretching absorption at 2114(m) and 2139(s) cm.$^{-1}$ and is probably the 6β-isomer by analogy with the configuration at C_6 of other cyclosteroids.[12]

The utility of the technique of infrared analysis with deuterium tracer to determine the stereochemistry of reactions in which carbon–hydrogen bonds are formed is further illustrated by certain replacement reactions of 3-halocholestanes. Reduction of 3β-iodocholestane[13] with zinc–deuteroacetic acid has been found to afford almost exclusively 3β-deuterocholestane (>95%) and only a small amount (probably less than 2%) of the 3α-deutero epimer. Decomposition of cholestanylmagnesium chloride by deuterium oxide or O-deuteroacetic acid also affords 3β-deuterocholestane almost exclusively (>95%). In the case of the cholestanyl Grignard reagent it seems likely that the solvated magnesium substituent is β-oriented (equatorial) and that electrophilic substitution by hydrogen takes place with retention of configuration.[14] The zinc–O-deuteroacetic acid reduction of 3β-iodocholestane may proceed similarly *via* a 3-zinc derivative or, alternatively, by concerted nucleophilic attack (by zinc) on iodine and electrophilic attack (by O-deuteroacetic acid) on carbon. In either event the substitution process would proceed with retention of configuration in the deuteration step.

Other examples of the application of the isotope analysis technique described above to stereochemical problems will be described later.

Experimental[15]

3α-Deuterocholestan-3β-ol Tosylate.—A solution of 1 g. of cholestanone and 0.5 g. of lithium aluminum deuteride in 80 ml. of dry ether was heated to reflux for 85 hours, cooled and treated with dilute sulfuric acid. Evaporation of the ether and chromatographic purification over alumina gave 0.90 g. of 3α-deuterocholestan-3β-ol, m.p. 137–138°, and 0.1 g. of 3β-deuterocholestan-3α-ol, m.p. 172–176°. The former (0.89 g.) was converted to the tosylate with 1.2 g. of tosyl chloride in 5 ml. of pyridine at room temperature for 24 hours. The tosylate was isolated by addition of ether, extraction with dilute hydrochloric acid, evaporation and crystallization from ether, m.p. 134–136°, 1.03 g. (83%).

3β-Deuterocholestane.—A mixture of 4 g. of lithium aluminum hydride and 0.96 g. of 3α-deuterocholestan-3β-ol tosylate in 120 ml. of dry ether was heated to reflux for seven days. The excess hydride was decomposed and the crude product was obtained by evaporation of an ethereal solution after washing with dilute acid and base. Purification was effected by chromatography over alumina followed by recrystallization from ether-methanol; yield 0.42 g. (63.7%), m.p. 77–78°.

3,3-Dideuterocholestane was obtained in the same way using 0.6 g. of lithium aluminum deuteride and 1.01 g. 3α-deuterocholestan-3β-ol tosylate, m.p. 77–78°.

3α-Deuterocholestane.—This material was prepared from 1.02 g. of cholestan-3β-ol tosylate and 0.40 g. of lithium aluminum deuteride in ethereal solution at reflux, m.p. 76.5–77.5°.

1-Deutero-*trans*-4-phenylcyclohexyl Tosylate.[16]—A solution of 0.5 g. of 4-phenylcyclohexanone, m.p. 77–78°, and 0.58 g. of lithium aluminum deuteride in ether was heated at reflux for 73 hours, decomposed with ethyl acetate and extracted with dilute acid. Evaporation of the ether and recrystallization of the residue from ligroin yielded 0.46 g. (93.8%) of 1-deutero-*trans*-4-phenylcyclohexanol, m.p. 118–119°. This alcohol was converted to the tosylate with a 3-fold amount of tosyl chloride in a minimum of pyridine to effect solution at 25° for 12 hours. Dilution with water and recrystallization of the solid from methanol afforded 0.75 g. (80.6%) of tosylate, m.p. 98.3–99.5°.

***trans*-4-Phenyldeuterocyclohexane.**—A mixture of 1 g. of 1-deutero-*trans*-4-phenylcyclohexyl tosylate and 0.28 g. of lithium aluminum hydride in 70 ml. of anhydrous ether was heated to reflux for 96 hours. Ethyl acetate was added to decompose the excess hydride and the ether layer was washed with 4 *N* hydrochloric acid, 10% sodium hydroxide solution and saturated salt solution. After drying over calcium chloride, the solution was concentrated and the liquid residue was chromatographed on a 33 × 1 cm. column of Merck alumina. *n*-Pentane eluted 0.332 g. (69%) of *trans*-4-phenyldeuterocyclohexane purified by evaporative distillation at 120° bath temperature (11.5 mm.), $n^{19.6}$D 1.5283.

***cis*-4-Phenyldeuterocyclohexane.**—This compound was prepared in the same manner as described for the *trans* isomer above from 0.66 g. of lithium aluminum deuteride and 1 g. of *trans*-4-phenylcyclohexyl tosylate in ether at reflux for 96 hours, $n^{19.6}$D 1.5280.

4,4-Dideuterophenylcyclohexane, n^{20}D 1.5280, was prepared from 1-deutero-*trans*-4-phenylcyclohexyl tosylate and lithium aluminum deuteride.

Lithium Aluminum Deuteride Reduction of Cholesteryl Tosylate.—A solution of 4.00 g. of cholesteryl tosylate in 35 ml. of dry benzene was added to a stirred refluxing solution of 1.40 g. of lithium aluminum deuteride in 225 ml. of ether and the solution was maintained at reflux temperature for 5 days. The excess deuteride was decomposed with ethyl acetate and the ethereal solution was washed with 2% sulfuric acid, 2% sodium hydroxide and finally with water. The ethereal solution was evaporated and the residue was dried by benzene distillation and then taken up in pentane and chromatographed carefully with a 80 × 1.5 cm. column of alumina using pentane and collecting 2-ml. fractions. In this way 0.8538 g. of 3-deutero-Δ⁵-cholestene, m.p. 77–79°, was obtained followed by 0.2663 g. of 6-deutero-3,5-cyclocholestane with a series of intermediate fractions containing 0.9368 g. of unresolved mixture. The 3-deutero-Δ⁵-cholestene showed infrared absorption at 2162 cm.$^{-1}$ (s) and 2177 cm.$^{-1}$ (shoulder)[17]; the 6-deutero-3,5-cyclocholestane showed absorption at 2114 cm.$^{-1}$ (m) and 2139 cm.$^{-1}$ (s).

The 3-deutero-Δ⁵-cholestene produced above (50 mg.) was hydrogenated in 10 ml. of cyclohexane–5 ml. of glacial acetic acid with 10 mg. of platinum catalyst. After 2 hours the catalyst was removed, the filtrate was evaporated and the residue was recrystallized from ether affording 28.5 mg. of 3-deuterocholestane, m.p. 78–79°, mixed m.p. with starting material 70–77°, mixed m.p. with 3β-deuterocholestane 78–79°. The infrared absorption of this material was identical

(12) C. W. Shoppee and G. R. Summers, *J. Chem. Soc.*, 3361 (1952).

(13) For evidence on iodine configuration see Experimental.

(14) *Cf.* the carbonation of cholestanylmagnesium chloride which produces cholestan-3β-carboxylic acid, E. J. Corey and R. A. Sneen, THIS JOURNAL, **75**, 6234 (1953); Roberts and C. W. Shoppee, *J. Chem. Soc.*, 3418 (1954). For the stereochemistry of mercury exchange with organomercurials see S. Winstein, T. G. Traylor and C. S. Garner, THIS JOURNAL, **77**, 3741 (1955).

(15) Elemental analyses by Mr. Jozsef Nemeth and associates.

(16) H. E. Ungnade, *J. Org. Chem.*, **13**, 361 (1948).

(17) The intensity of this band is erroneously given as med. in ref. 4.

with that of authentic 3β-deuterocholestane and hence the unsaturated reduction product of cholesteryl tosylate must be 3β-deutero-Δ⁵-cholestene.

3β-Iodocholestane.[18]—Cholestan-3β-ol was prepared conveniently by catalytic reduction of cholesterol (25 g.) in ether (300 ml.) containing 72% perchloric acid (*ca.* 0.5 ml.) with platinum catalyst and hydrogen in a low pressure apparatus. The product was isolated in 98% yield by filtration, concentration of the ether solution and crystallization from ether–ethanol; m.p. 139.5–140°. Cholestan-3β-ol tosylate was prepared from the alcohol as described above and was converted on a 6-g. scale to 3β-iodocholestane by heating with sodium iodide (12 g.) in 200 ml. of dry acetone at 100° in a pressure bottle for 30 minutes. The reaction mixture was concentrated, taken up in ether–water and the ether solution was washed with water, sodium thiosulfate solution and saturated salt solution, and evaporated to dryness. The crude product was purified by filtration in cyclohexane solution through a column of alumina and subsequent recrystallization from acetone–methanol, m.p. 105.5–106.5°, $[\alpha]^{30}D$ +31.4°.

Anal. Calcd. for $C_{27}H_{47}I$: C, 65.09; H, 9.51; I, 25.60. Found: C, 64.78; H, 9.37.

The β-orientation of iodine in the above product (for proof see below) is probably the result of displacement by iodine ion on 3α-iodocholestane, which is undoubtedly the primary product, to give the thermodynamically more stable product with iodine equatorial. The above product is not subject to epimerization by further treatment with iodide ion in acetone at 100° for 4 hours.

Conversion of 3β-Iodocholestane and Cholestan-3β-ol Tosylate to 3α-Thiocyanocholestane.—The 3β-iodo and tosyloxy derivatives of cholestane were treated with a large excess of potassium thiocyanate in concentrated ethanol solution at reflux for 26 hours. Both starting materials gave the same thiocyanate, m.p. and mixed m.p. 95.5–96° after recrystallization from methanol–water (yield 70–78%).

Anal. Calcd. for $C_{27}H_{45}SN$: C, 77.63; H, 11.34; S, 7.67. Found: C, 77.98; H, 10.97; S, 7.47.

Zinc–O-Deuteroacetic Acid Reduction of 3β-Iodocholestane.—A solution of 150 mg. of 3β-iodocholestane in 5 ml. of anhydrous ether and 3.5 ml. of O-deuteroacetic acid was heated and stirred at reflux with 0.8 g. of zinc dust for 24 hours. Filtration, evaporation of the solvent and recrystallization from ether–absolute ethanol gave 3β-deuterocholestane, m.p. 81–82°, containing little or no 3α-deutero epimer as judged by infrared analysis.

Deuteration of Cholestanylmagnesium Chloride.—A solution of cholestanylmagnesium chloride was prepared by treating 0.70 g. of magnesium powder in 10 ml. of ether with 0.25 ml. of ethyl bromide at reflux under nitrogen followed by a solution of 2.0 g. of cholestanyl chloride in 35 ml. of ether which was added dropwise over 3 hours. The solution was refluxed for 24 hours, cooled and filtered in equal parts (a) into a solution of 1.2 g. of O-deuteroacetic acid in 20 ml. of ether and (b) a solution of 0.3 g. of deuterium oxide in ether. The 3-deuterocholestane produced in each case was isolated by washing the reaction mixture with aqueous acid, evaporation of the ethereal solution and recrystallization from ether–acetone; m.p. 79–80°. Infrared analysis of these samples revealed each to be essentially 3β-deuterocholestane with no detectable 3α-deutero epimer (<5%).

Zinc–O-Deuteroacetic Acid Debromination of 5α- and 7α-Bromo-3β-acetoxycholestan-6-one.—A solution of 170 mg. of the 5α- or 7α-bromoketone[19] in 25 ml. of anhydrous ether and 7 g. of O-deuteroacetic acid was stirred at room temperature for 18 hours with 0.60 g. of zinc dust. The product was isolated in each case by filtration, evaporation and recrystallization from methylene chloride–methanol; m.p. 128–129°. The 5α-deutero-3β-acetoxylcholestan-6-one produced from the 5α-bromoketone showed C–D stretching absorption at 2128 cm.$^{-1}$ and the 7α-deutero-3β-acetoxycholestan-6-one produced from the 7α-bromoketone showed absorption at 2138 cm.$^{-1}$. The α-orientation of deuterium in the latter product seems most likely on the basis of experiments to be published in a separate paper.[21]

2β-Deuterocholestan-3α-ol.—To a solution of 534 mg. of 2,3α-oxidocholestane, m.p. 104.5–105°,[20] in 40 ml. of absolute ether was added 105 mg. of lithium aluminum deuteride, and the reaction mixture was heated to reflux for 110 hours. The steroid was isolated in the usual way and was recrystallized from ethanol–water affording 360 mg. of 2β-deuterocholestan-3α-ol, m.p. 181–183°, infrared absorption at 2161, 2171 cm.$^{-1}$.

2β-Deuterocholestan-3-one.—To a solution of 128 mg. of 2β-deuterocholestan-3α-ol in 6 ml. of benzene (cooled to 5°) was added an ice-cold solution of 0.25 g. of chromium trioxide, 0.25 g. of sodium dichromate and 0.4 ml. of acetic acid in 2 ml. of water. The temperature of the reaction mixture was allowed to rise slowly to a maximum of 13° (tap-water cooling) and the reaction mixture was maintained at that temperature for 17 hours. The water layer was removed and the benzene solution was washed successively with cold water, twice with cold 2% sodium hydroxide and finally with water. Evaporation of the benzene under reduced pressure and recrystallization from ethanol–water afforded 87 mg. of 2β-deuterocholestan-3-one, m.p. 129.5–130.2°. A single band at 2145 cm.$^{-1}$ was found in the C–D stretching region of the infrared spectrum.

Reduction of 2α-bromocholestan-3-one with zinc–O-deuteroacetic acid afforded a 2-deuterocholestan-3-one with infrared absorption identical with that obtained for the 2β-deutero-3-ketone described above. Further reduction with lithium aluminum hydride afforded 2-deuterocholestan-3β-ol and 2-deuterocholestan-3α-ol (separated by chromatography). The infrared absorption of the latter was identical with that of authentic 2β-deuterocholestan-3α-ol which indicates that the deuterium atom introduced at the 2-position by zinc–O-deuteroacetic acid reduction of 2-bromocholestan-3-one is β-oriented.[21]

Measurement of Infrared Spectra.—The measurements reported herein were obtained both with a Perkin–Elmer, single-beam, double pass spectrophotometer with a high dispersion lithium fluoride prism (accuracy ±1 cm.$^{-1}$) and with a Perkin–Elmer double beam spectrophotometer, Model D 11 (accuracy ±2 cm.$^{-1}$). Considerably better resolution was achieved with the single beam instrument. A four-expansion of the normal wave number scale was employed with the D-11 instrument. All measurements were made in carbon tetrachloride or in a few cases chloroform solution. Carbon disulfide absorbs too strongly in the C–D stretching region to be of value. The infrared data reported herein were obtained by Messrs. R. L. Rutledge, R. Bohon and J. Brader.

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(18) Experiment performed by W. J. Wechter.

(19) E. J. Corey, THIS JOURNAL, **76**, 175 (1954).

(20) A. Fürst and Pl. A. Plattner, *Helv. Chim. Acta*, **32**, 275 (1949).

(21) For evidence that the reaction of α-bromo ketones with zinc–O-deuteroacetic acid proceeds by way of the enol with subsequent deuteration and not by direct displacement see E. J. Corey and R. A. Sneen, THIS JOURNAL, in press.