Some Conformational Aspects of Neighbouring-group Participation.

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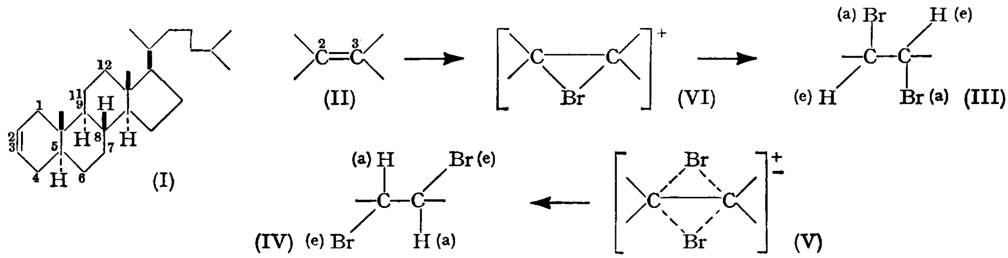
The addition of chlorine or bromine to *cyclo*hexene systems affords, as main product, the diaxial dihalide. This generalisation is illustrated by the addition reactions of cholest-2- and -3-ene as well as by material already published.

Phenomena due to neighbouring-group participation have been studied with diequatorial and diaxial bromo- and chloro-hydrins based on cholest-2-ene. Only the diaxial halogenohydrins show neighbouring-group participation. With diaxial bromohydrins there is clear evidence of participation with all reagents studied. With the chlorohydrins participation depends not only on the geometry of the system but also on the reagent. The results demonstrate that halogenohydrin replacement reactions proceed with maximum ease when the centres of importance in the reaction are coplanar.

Corresponding pairs of 2 : 3-dihalogenocholestanes are isomorphous.

BEFORE proceeding to the main substance of this paper it is imperative to discuss the stereochemical course of halogen addition to *cyclo*hexenes, in particular addition to cholest-2-ene (I). Addition of bromine to the 11 : 12-ethylenic linkage of certain bile acid derivatives affords mainly the 11β : 12α-dibromide (Turner, Mattox, Engel, McKenzie, and Kendall, *J. Biol. Chem.*, 1946, **166** 345). Addition of either chlorine or bromine to the 5 : 6-ethylenic linkage of cholesterol and its congeners gives the 5α : 6β-dihalides (Barton and Miller *J. Amer. Chem. Soc.*, 1950, **72**, 370, 1066) as sole isolated products. It seemed to us, *ab origine*, that in each of these cases the addition afforded mainly the diaxial dihalide and that preferential diaxial addition of halogen to *cyclo*hexene systems might be a general rule. The addition reactions studied in the present work are summarised in Table 1 and support this proposal.

The configurations assigned are based on the generally accepted principle that addition of halogen is of *trans*-ionic type and on the following considerations. Addition of bromine to cholest-2-ene (I), which may be represented by partial symbol (II) *, gave mainly the known dibromide, m. p. 123—124°, which was regarded by Barton and Rosenfelder



(*J.*, 1951, 1048) as the (diaxial) 2β : 3α-derivative (III). This configuration is confirmed by the fact that on melting the compound rearranges to a more stable (diequatorial) dibromide (IV), m. p. 144—145° (Hattori and Kawasaki, *J. Pharm. Soc. Japan*, 1937, **57**, 115, 588). On debromination with zinc the latter compound afforded cholest-2-ene. The mechanism of this rearrangement must be comparable to that, (V), established by Grob and Winstein (*Helv. Chim. Acta*, 1952, **35**, 782) for the rearrangement of the 5α : 6β-dibromide of cholest-5-ene to the 5β : 6α-dibromide (Barton and Miller, *loc. cit.*). If the starting dibromide is one (the diaxial 2β : 3α) of the pair of *trans*-dibromides from cholest-2-ene, the other (diequatorial, 2α : 3β-)*trans*-dibromide must be formed in the above rearrangement. In agreement the rearranged dibromide is the minor product of the (*trans*-)addition of bromine to cholest-2-ene. The relative rates of debromination of the two dibromides (see Table 2) provide strong support for these configurations on the basis of the now generally accepted interplay of conformation and configuration (see Barton, *Experientia*, 1950, **6**, 316; Barton and Rosenfelder, *loc. cit.*; Barton, *J.*, 1953, 1027).

TABLE 1.

Addition of halogen to	Halogen added	Solvent	Yields (adjusted to add up to 100%) * Diaxial	Diequatorial	Ratio, diaxial : diequatorial
			2β : 3α-	2α : 3β-	
Cholest-2-ene	Cl_2	CCl_4	72	28	2·6
	Br_2	CCl_4	88	12	7·3
	Br_2	$AcOH-Et_2O$	91	9	10
			3α : 4β-	3β : 4α-	
Cholest-3-ene	Br_2	CCl_4	97	3	32

* The actual total yields in these four experiments were 76, 84, 77, and 81% respectively.

The addition of bromine to cholest-3-ene gave (see Table 1) mainly a dibromide, m. p. 124—126°, which had already been prepared in the same way by Barton and Rosenfelder (*loc. cit.*).† This must be the diaxial 3α : 4β-dibromide for when heated it rearranged to

* Such partial symbols represent a broadside view in the main plane of the steroid nucleus from outside the molecule and perpendicular to the bond (here C_2–C_3) under consideration.

† Barton and Rosenfelder (*loc. cit.*) tentatively regarded this compound as the (diequatorial) 3β : 4α-dibromide because of its slow debromination relative to (diaxial) 2β : 3α- and 11β : 12α-dibromides. Their observation is correct but the inference drawn must be qualified now that both (*trans*-)3 : 4-dibromides of cholest-3-ene are available. The sluggish debromination (see Table 2) of 3α : 4β- relative to 2β : 3α-dibromocholestane is in agreement with the fact that it is harder (in a *trans*-A/B system) to enolise a $C_{(3)}$-ketone towards $C_{(4)}$ than towards $C_{(2)}$.

a second dibromide (which was the minor product of the addition reaction), m. p. 171—173°. This must be the more stable (diequatorial) 3β : 4α-dibromide. It gave back cholest-3-ene on debromination with zinc dust. The relative rates of debromination (see Table 2) of the two dibromides confirmed the assigned configurations.

The addition of chlorine to cholest-2-ene in carbon tetrachloride afforded two dichlorides, (main product) m. p. 108—112°, $[\alpha]_D$ +63°, and (minor product) m. p. 150—152°, $[\alpha]_D$ −7°. These are assigned the 2β : 3α- and the 2α : 3β-configuration respectively for the following reasons. (i) The rotations correspond to those recorded for the 2β : 3α- and 2α : 3β-dibromide. (ii) We find it a rule that pairs of diaxial dichlorides and dibromides (for example, those based on cholesterol) are isomorphous and give no m. p. depression and the same would be expected to hold for the diequatorial compounds. Thus 2β : 3α-dichloro- and -dibromo-cholestane give no depression, nor do the 2α : 3β-dichloro- and -dibromo-compounds. But all possible combinations of the 2β : 3α- and 2α : 3β-derivatives give marked depressions. (iii) The 2β : 3α(diaxial)-dichloride is readily dechlorinated by zinc to give the parent hydrocarbon. The 2α : 3β(diequatorial)-compound does not lose halogen nearly so readily, although it also affords cholest-2-ene.

During these studies the interesting observation was made that addition of the halogen in a solvent containing acetic acid, with or without sodium acetate, gave as main product the diaxially substituted 3α-chlorocholestan-2β-yl acetate together with approximately equal amounts of the two (*trans*-)dichlorides. The constitution of the acetate is established by its conversion into 2β : 3β-epoxycholestane with alkali and by its preparation from authentic 3α-chlorocholestan-2β-ol (see below) by acetylation. A comparable phenomenon was not observed in bromine addition. The addition of the chlorine was notably less stereospecific (see Table 1) than that of bromine.

If one regards halogen addition as proceeding through a three-membered intermediate [for example, as in (VI); see de la Mare, *Ann. Reports*, 1950, **47**, 126; Ingold, " Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, 1953, pp. 658 *et seq.*], then diaxial halogen addition would be expected since the intermediate resembles, at least

TABLE 2. *Rates of debromination of dibromides.**

Dibromo-cholestane	Molarity	Percentage reacted
2β : 3α- (at 20°)	0·00572	7 (3 days), 14 (10 days), 43 (25 days), 77 (59 days)
2α : 3β- (at 20°)	0·00495	0 (3 days), 0 (59 days)
3α : 4β- † (at 40°)	0·00640	10 (2 days), 21 (4 days), 91 (14 days)
3β : 4α- ‡ (at 40°)	0·00557	0 (2 days), 0 (4 days), 1 (14 days)

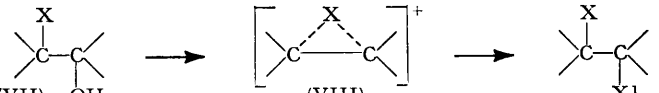
* The rates of debromination were measured as described by Barton and Rosenfelder (*loc. cit.*).
† 2% debromination after 28 days at 20°. ‡ 0·0% debromination after 28 days at 20°.

geometrically, an ethylene oxide. Diaxial opening of the latter is well established (Fürst and Plattner, Abs. Papers, p. 409, 12th Internat. Congr. Pure Appl. Chem., New York, 1951; see Barton, *loc. cit.*, and further below).

The elegant investigations by Winstein and his colleagues (series of papers in the *J. Amer. Chem. Soc.*, on " The Role of Neighbouring Groups in Replacement Reactions ") on the stereochemical course of (*inter alia*) the replacement reactions of halogenohydrins have not hitherto been considered from the conformational point of view. It appears, however, to be generally understood (cf. Winstein and Heck, *ibid.*, 1952, **74**, 5584, and references there cited) that the geometrical requirement for maximum ease of neighbouring-group participation is that the centres of importance in the reaction should be as near coplanarity as possible. We are now able to provide experimental support for this hypothesis.

If the participation of the neighbouring halogen atom (X) be represented as in (VII) ⟶ (VIII) ⟶ (IX), then the geometrical condition for maximum participation will be that Cα, Cβ, the O of OH and X should be coplanar. In *cyclo*hexane derivatives it is now well appreciated that this condition is satisfied if X and OH are both axial, but *not* if X and OH are both equatorial or if X and OH are severally axial and equatorial. The first two arrangements correspond to *trans*-1 : 2-disubstituted *cyclo*hexanes, the last two to *cis*-compounds.

Table 3 summarises a number of experiments carried out on pairs of diaxial and diequatorial chloro- and bromo-hydrins based on cholest-2-ene. We discuss first the replacement reactions of the bromohydrins. In every case the replacement reaction proceeds smoothly with the diaxial bromohydrin, but takes a different course with the



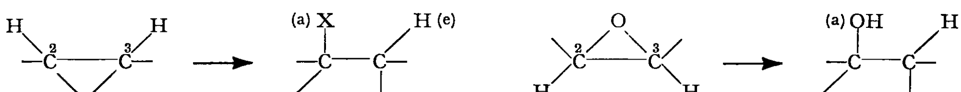
(VII) (VIII) (IX)

diequatorial compound. In addition to the results summarised in Table 3 we have also shown (see Experimental section) that 2β-bromocholestan-3α-ol is smoothly converted into the diaxial 2β : 3α-dibromide with phosphorus pentabromide, and that the diequatorial 2α-bromocholestan-3β-ol is recovered unchanged. More vigorous treatment than that outlined in Table 3 of 2β-bromocholestan-3α-ol with hydrobromic–acetic acid afforded the 2α : 3β-dibromide by rearrangement of the 2β : 3α-compound initially formed. Under the same vigorous conditions 2α-bromocholestan-3β-ol was still only converted into its acetate.

With the chlorohydrins it was clearly established by the products of reaction that participation was determined, not only by the geometry of the system, but also by the substituting reagent. Thus the diaxial 2β-chlorocholestan-3α-ol underwent smoothly replacement of hydroxyl by chlorine in reaction with phosphorus pentachloride, whilst the diequatorial 2α-chlorocholestan-3β-ol gave a complex mixture. Both chlorohydrins gave only the corresponding acetates on treatment with hydrobromic–acetic acid.

Corresponding observations (see Table 3) were made with the diaxial 3α-bromo- and 3α-chloro-cholestan-2β-ol. The bromohydrin exhibited smooth neighbouring-group participation with all reagents, whereas the chlorohydrin exhibited participation with phosphorus pentachloride but not with hydrobromic acid. The different behaviour of chloro- and bromo-hydrins is not unexpected (cf. Winstein and Grunwald, *ibid.*, 1948, **70**, 828, and references cited there).

The discussion based on Table 3 assigns configurations to numerous 2 : 3-disubstituted cholestanes, and these assignments must now be justified. The 2β-bromo- and 2β-chloro-cholestan-3α-ols were prepared by opening 2α : 3α-epoxycholestane (X) with the appropriate halogen acid (HX). The diaxial opening rule predicts the course of this reaction (to give XI). In confirmation, chromic acid oxidation of 2β-chlorocholestan-3α-ol gave 2β-chlorocholestan-3-one, which was smoothly reduced by zinc dust to cholestan-3-one. Similar oxidation of 2β-bromocholestan-3α-ol afforded 2β-bromocholestan-3-one; this was not obtained in a satisfactorily crystalline state, but it rearranged smoothly on filtration over alumina to the well-known 2α-bromocholestan-3-one (see Fieser and Huang, *ibid.*, 1953, **75**, 4837; Corey, *ibid.*, p. 4833; and references cited there). Corresponding opening of 2β : 3β-epoxycholestane (XII) with halogen acid (HX) gave halogenohydrins predicted by the diaxial

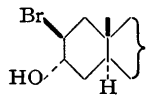
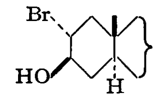
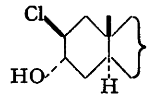
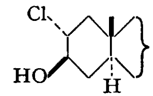
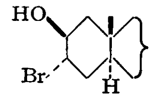
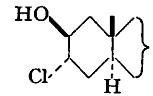
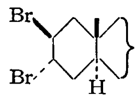
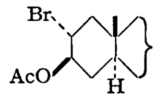
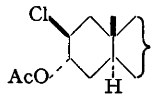
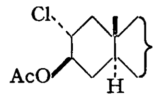
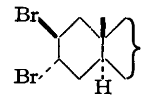
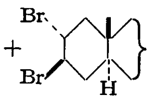
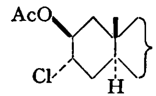
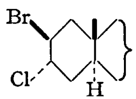
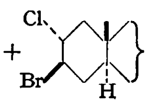
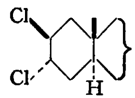
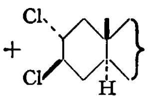
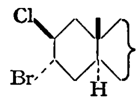
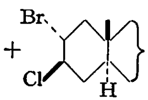
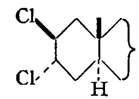
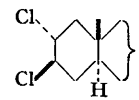
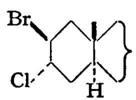
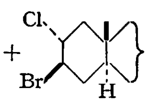
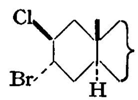
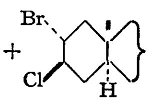


(X) (XI) (XII) (XIII)

opening rule to have constitution (XIII). In agreement, chromic acid oxidation of 3α-chloro- and 3α-bromo-cholestan-2β-ol gave, respectively, 3α-chloro- and 3α-bromo-cholestan-2-one. Both these ketones showed the expected normal carbonyl bands at 1714 and 1715 cm.$^{-1}$ respectively. Cholestan-2-one itself absorbed at 1712 cm.$^{-1}$. Reduction of both halogeno-ketones by zinc dust furnished cholestan-2-one.

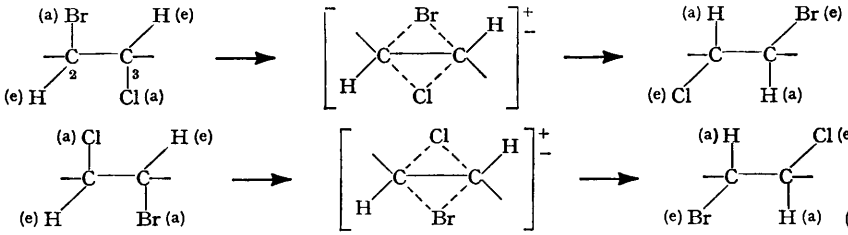
The configurations of 2α-bromo- and 2α-chloro-cholestan-3β-ol have already been established (Fieser and Huang, *J. Amer. Chem. Soc.*, *loc. cit.*; Corey, *loc. cit.*; Beereboom, Djerassi, Ginsburg, and Fieser, *ibid.*, p. 3500). The configurations of the dichlorides and dibromides produced have also been established (see above). There remains for consideration a justification of the configurations assigned to the four mixed chloro-bromides.

TABLE 3. *Product(s) from halogenohydrins (yields in parentheses).*

Reagent	 (diaxial)	 (diequatorial)	 (diaxial)	 (diequatorial)	 (diaxial)	 (diaxial)
HBr–AcOH at room temp.	 (65%)	 (47%)	 (70%)	 (80%)	 (66%) +  (6%)	 (73%)
PCl_5 in boiling C_6H_6	 (68%) +  (20%)	Complex mixture	 (62%) +  (17%)	Complex mixture	 (77%) +  (8%)	 (78%)  (6%)
$SOCl_2$ at room temp.	 (60%) +  (22%)	No reaction : recovered unchanged (68%)	—	No reaction : recovered unchanged (75%)	 (72%) +  (7%)	—

These are based on the established configurations of the precursors, on the well-accepted principle of Winstein *et al.* (*loc. cit.*) that participation is only possible with *trans*-oriented substituents and must necessarily afford *trans*-products, on the magnitudes of the rotations and on the isomorphism of the compounds with respect to the dichlorides and dibromides of corresponding configurations. Thus the diaxial chloro-bromides gave no m. p. depression with either 2β : 3α-dichloro- or -dibromo-cholestane, but gave a depression with the diequatorial analogues. Corresponding observations were made with the diequatorial chloro-bromides. In agreement also, thermal rearrangement of 2β-bromo-3α-chlorocholestane

(XIV)



(XV)

(XVI) (XVII)

(XIV) gave the more stable diequatorial 2α-chloro-3β-bromocholestane (XV), whilst similar treatment of the diaxial 2β-chloro-3α-bromocholestane (XVI) afforded the more stable 2α-bromo-3β-chlorocholestane (XVII). The appropriate model experiments were,

TABLE 4. *Contribution of the halogen atoms to* $[M]_D$.*

2 : 3-*Dihalides.*		5 : 6-*Dihalides.*	
2β : 3α-Dibromocholestane	+311°	5α : 6β-Dibromocholestane	−298°
2β : 3α-Dichlorocholestane	+168	5α : 6β-Dichlorocholestane	−215
2β-Bromo-3α-chlorocholestane	+234	5α-Bromo-6β-chlorocholestan-3β-yl benzoate	−306
2β-Chloro-3α-bromocholestane	+210		
2α : 3β-Dibromocholestane	−245		
2α : 3β-Dichlorocholestane	−120		
2α-Bromo-3β-chlorocholestane	−174		
2α-Chloro-3β-bromocholestane	−169		

* Based on cholestane or the appropriate cholestane derivative as reference compound.

of course, carried out to show that such rearrangements were not complicating the course of the replacement reactions summarised in Table 3.

Mention has several times been made in the above discussion of a similarity in rotation of dihalides of similar configuration. The evidence justifying this assertion is set out briefly in Table 4.

EXPERIMENTAL

For general experimental details see *J.*, 1952, 2339. Rotations were determined in chloroform solution at room temperature. The light petroleum used had b. p. 40—60°. The alumina for chromatography was Spence's Grade H; solutions for chromatography were prepared in light petroleum.

Cholest-2-ene.—The following procedure is superior to that of Fürst and Plattner (*Helv. Chim. Acta*, 1949, **32**, 279) and avoids purification *via* the dibromide. 2α-Bromocholestan-3-one (Butenandt and Wolff, *Ber.*, 1935, **68**, 2091) (9 g.) was treated with sodium borohydride (900 mg.) in absolute ethanol (see Fieser and Huang, *J. Amer. Chem. Soc.*, 1953, **75**, 4837) at room temperature for 24 hr., during which the ketone slowly dissolved. The total product, in "AnalaR" acetic acid (150 ml.), was refluxed with zinc dust (10 g.; added portionwise) for 1 hr. (cf. Fieser and Dominguez, *ibid.*, p. 1704). Filtration through alumina (160 g.) in light petroleum and crystallisation from ethyl acetate–methanol then gave pure cholest-2-ene (4·2 g.) as needles, m. p. 74—75°, $[\alpha]_D$ +66° (*c*, 1·65).

Bromination of Cholest-2-ene.—(a) *In* 1 : 1 *ether–acetic acid.* Cholest-2-ene (370 mg.) in 1 : 1 dry ether–"AnalaR" acetic acid (25 ml.) was titrated with a solution of bromine in "AnalaR" acetic acid (40 mg. per ml.). The uptake during 2 hr. at room temperature was equivalent to 1·13 mols. of bromine. The total product was chromatographed over alumina (16 g.). Elution with light petroleum (150 ml.) gave 2β : 3α-dibromocholestane (370 mg., 70%)

as plates (from ethyl acetate–methanol), m. p. 123—124°, $[\alpha]_D$ +76° (*c*, 2·17). Further elution with 9 : 1 and 5 : 1 light petroleum–benzene (100 and 50 ml. respectively) afforded 2α : 3β-dibromocholestane (37 mg., 7%) as needles (from ethyl acetate–methanol), m. p. 144—145°, $[\alpha]_D$ −30° (*c*, 1·69), undepressed in m. p. on admixture with the authentic material described below. To show that the 2β : 3α-dibromide did not isomerise to the 2α : 3β-compound during the working up, the 2β : 3α-dibromide (190 mg.) was subjected to the same treatment as in the working up of the total bromination product. Chromatography over alumina gave the 2β : 3α-dibromide {m. p. 123—124°, $[\alpha]_D$ +76° (*c*, 2·46)} and no trace of the epimeric dibromide.

(b) *In carbon tetrachloride.* Cholest-2-ene (185 mg.) in carbon tetrachloride (2 ml.) was titrated with a solution of bromine in the same solvent (40 mg. per ml.) at room temperature. The uptake (during 1 hr.) was equivalent to 1·10 mols. of bromine. The total product was chromatographed over alumina (7 g.). Elution with light petroleum gave the 2β : 3α-dibromide (195 mg., 74%), m. p. 122—124°, $[\alpha]_D$ +77° (*c*, 2·44), whilst elution with 9 : 1 light petroleum–benzene afforded the 2α : 3β-dibromide (26 mg., 10%), m. p. 144—145°, $[\alpha]_D$ −29° (*c*, 1·82).

2α : 3β-*Dibromocholestane* (cf. Hattori and Kawasaki, *J. Pharm. Soc. Japan*, 1937, **57**, 115, 588).—2β : 3α-Dibromocholestane (500 mg.) was heated in nitrogen at 185° for 20 min. The product, crystallised twice from ethyl acetate–methanol, was pure 2α : 3β-dibromide (400 mg.), m. p. 144—145° (needles), $[\alpha]_D$ −29° (*c*, 1·32). This dibromide (140 mg.) in " AnalaR " acetic acid (15 ml.) was heated for 1 hr. on the steam-bath with zinc dust (1 g.; added portionwise) to give cholest-2-ene (68 mg., 70%), m. p. 74—75° (from ethyl acetate–methanol), $[\alpha]_D$ +67° (*c*, 1·59), undepressed in m. p. on admixture with authentic cholest-2-ene (see above).

Chlorination of Cholest-2-ene.—(a) *In carbon tetrachloride.* Cholest-2-ene (370 mg.) in carbon tetrachloride (10 ml.) was titrated with a solution of chlorine in the same solvent (36 mg. per ml.). Approx. 1·10 mols. of chlorine were rapidly consumed (20 min.) at room temperature. The total product was chromatographed over alumina (14 g.). Elution with light petroleum (100 ml.) gave 2β : 3α-*dichlorocholestane* (240 mg., 55%), fine needles (from ethyl acetate–methanol), m. p. 108—112°, $[\alpha]_D$ +63° (*c*, 1·90) (Found: C, 73·25; H, 10·85; Cl, 15·7. $C_{27}H_{46}Cl_2$ requires C, 73·45; H, 10·5; Cl, 16·05%). The physical constants were unchanged on repeated recrystallisation and on further chromatography. Further elution with light petroleum (150 ml.) afforded 2α : 3β-*dichlorocholestane* (91 mg., 21%), prismatic needles (from chloroform–methanol), m. p. 150—152°, $[\alpha]_D$ −7° (*c*, 1·76) (Found: C, 73·4; H, 10·6; Cl, 16·3. $C_{27}H_{46}Cl_2$ requires C, 73·45; H, 10·5; Cl, 16·05%).

(b) *In the presence of acetic acid.* Cholest-2-ene (185 mg.) in 1 : 3 carbon tetrachloride–" AnalaR " acetic acid (5 ml.) was titrated with a solution of chlorine in carbon tetrachloride (36 mg. per ml.) at room temperature. Approx. 1·5 mols. of chlorine were rapidly (20 min.) consumed. The total product was chromatographed over alumina (7 g.). Elution with light petroleum (55 ml.) gave 2β : 3α-dichlorocholestane (22 mg., 10%), m. p. and mixed m. p. 108—112°, $[\alpha]_D$ +63° (*c*, 1·92). Further elution with light petroleum (100 ml.) furnished 2α : 3β-dichlorocholestane (22 mg., 10%), m. p. and mixed m. p. 150—152°, $[\alpha]_D$ −6° (*c*, 2·00). Elution with 4 : 1 light petroleum–benzene (125 ml.) afforded 3α-*chlorocholestan*-2β-*yl acetate* (130 mg., 56%), blades (from chloroform–methanol), m. p. 124—126°, $[\alpha]_D$ +63° (*c*, 2·16) (Found: C, 74·85; H, 11·05; Cl, 7·75. $C_{29}H_{49}O_2Cl$ requires C, 74·9; H, 10·6; Cl, 7·6%). There was a marked depression in m. p. on admixture with 2β-chlorocholestan-3α-yl acetate (see below), but no depression on admixture with the acetate of 3α-chlorocholestan-2β-ol (see below) of established constitution.

(c) *In the presence of sodium acetate.* Cholest-2-ene (185 mg.) in carbon tetrachloride (2 ml.) and " AnalaR " acetic acid (5 ml.) containing sodium acetate (200 mg.) was titrated at room temperature with a solution of chlorine in carbon tetrachloride (30 mg. per ml.). Approx. 1·25 mols. of chlorine were rapidly (20 min.) consumed. The total product was chromatographed over alumina (7 g.) as detailed under (*b*), to give 2β : 3α-dichlorocholestane (26 mg., 12%), m. p. and mixed m. p. 108—112°, $[\alpha]_D$ +61° (*c*, 1·27), 2α : 3β-dichlorocholestane (20 mg., 9%), m. p. and mixed m. p. 150—152°, $[\alpha]_D$ −6° (*c*, 1·06), and 2α-chlorocholestan-2β-yl acetate (130 mg., 56%), m. p. and mixed m. p. 124—126°, $[\alpha]_D$ +63° (*c*, 2·10).

2α : 3β-Dichlorocholestane (40 mg.) in " AnalaR " acetic acid (5 ml.) was heated under reflux with zinc dust (200 mg.; added portionwise) during 1½ hr. Crystallisation of the product from ethyl acetate–methanol gave cholest-2-ene (22 mg.), m. p. and mixed m. p. 74—75°, $[\alpha]_D$ +64° (*c*, 1·50).

2β : 3α-Dichlorocholestane (100 mg.) in " AnalaR " acetic acid (10 ml.) was treated with zinc dust (1·0 g.; added portionwise) on the steam-bath for 90 min. Crystallisation of the product from ethyl acetate–methanol gave cholest-2-ene (70 mg.; Beilstein test negative), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +65° (*c*, 2·05)}, and crystal form. In a comparable experiment 2α : 3β-dichlorocholestane (50 mg.) was recovered unchanged (45 mg.) and identified by m. p., mixed m. p., rotation {$[\alpha]_D$ −7° (*c*, 2·48)}, and crystal form.

3α-Chlorocholestan-2β-yl acetate (50 mg.) was heated at 55—60° for 1 hr. with *iso*propanolic potassium hydroxide (4%; 7 ml.). Crystallisation of the product from ether–methanol gave 2β : 3β-epoxycholestane, m. p. and mixed m. p. (see below) 89—91°, $[\alpha]_D$ +55° (*c*, 1·88).

2β-*Bromocholestan*-3α-*ol*.—2α : 3α-Epoxycholestane (500 mg.), m. p. 103—105°, $[\alpha]_D$ +37° (*c*, 2·14), prepared according to Fürst and Plattner (*Helv. Chim. Acta*, 1949, **32**, 279), in chloroform (30 ml.) was shaken with aqueous hydrobromic acid (50%; 10 ml.) for 7 min. (cf. Barton and Miller, *J. Amer. Chem. Soc.*, 1950, **72**, 1066). Washing with dilute sodium sulphite solution and with water and evaporation *in vacuo* afforded 2β-*bromocholestan*-3α-*ol* (from ether–methanol), m. p. 115—118°, $[\alpha]_D$ +44° (*c*, 1·49) (Found: C, 69·7; H, 9·95; Br, 17·2. $C_{27}H_{47}OBr$ requires C, 69·35; H, 10·0; Br, 17·1%). Treatment of this bromohydrin with pyridine and acetic anhydride (excess) overnight at room temperature gave 2β-*bromocholestan*-3α-*yl acetate*, blades (from acetone–methanol), m. p. 120—122°, $[\alpha]_D$ +71° (*c*, 2·13) (Found: C, 68·45; H, 9·8; Br, 16·0. $C_{29}H_{49}O_2Br$ requires C, 68·35; H, 9·7; Br, 15·7%).

2β-Bromocholestan-3α-ol (132 mg.) in "AnalaR" acetic acid (12 ml.) was treated with chromium trioxide (23 mg.) in the minimum of water at room temperature overnight. The product, precipitated from methanol by addition of water, had m. p. 104—106°, $[\alpha]_D$ +110° (*c*, 1·05). The high positive rotation (see the corresponding chloro-ketone) shows that this was the 2β-bromo-compound, but it could not be recrystallised satisfactorily. Filtration in benzene through alumina (3 g.) and crystallisation from acetone–methanol gave 2α-bromocholestan-3-one, identified by m. p., mixed m. p. and rotation {$[\alpha]_D$ +42° (*c*, 2·12)}.

Reactions of 2β-*Bromocholestan*-3α-*ol*.—(a) *With hydrobromic acid*. 2β-Bromocholestan-3α-ol (100 mg.) in chloroform (2 ml.) was treated with 50% hydrobromic acid in acetic acid (3 ml.) at room temperature for 4 days. The total product was filtered through alumina (3 g.) in light petroleum solution, to give 2β : 2α-dibromocholestane (74 mg., 65%), m. p. and mixed m. p. 122—124°, $[\alpha]_D$ +76° (*c*, 1·37).

Similarly 2β-bromocholestan-3α-ol (100 mg.) in chloroform (1 ml.) was heated with the same reagent (3 ml.) in a sealed tube at 100° for 4 hr. Worked up in the same way, the product was identified as 2α : 3β-dibromocholestane (79 mg., 70%), m. p. and mixed m. p. 143—145°, $[\alpha]_D$ −29° (*c*, 2·03).

(b) *With phosphorus pentabromide*. 2β-Bromocholestan-3α-ol (200 mg.) in dry "AnalaR" benzene (20 ml.) was refluxed with phosphorus pentabromide (200 mg.) for 1 hr. After addition of water (10 ml.) the mixture was refluxed for a further 15 min., and the benzene layer separated, washed with water, and evaporated *in vacuo*. The total product was chromatographed over alumina (7 g.), to give 2β : 3α-dibromocholestane (156 mg., 68%), m. p. and mixed m. p. 122—124°, $[\alpha]_D$ +76° (*c*, 2·07).

(c) *With phosphorus pentachloride*. 2β-Bromocholestan-3α-ol (200 mg.) in dry "AnalaR" benzene (20 ml.) was refluxed with phosphorus pentachloride (200 mg.) for 30 min. Worked up as described under (b) above, the product was then chromatographed over alumina (7 g.). Elution with light petroleum (100 ml.) gave 2β-*bromo*-3α-*chlorocholestane* (142 mg., 68%), plates (from ethyl acetate–methanol), m. p. 130—132°, $[\alpha]_D$ +66° (*c*, 2·90) (Found: C, 67·1; H, 9·6; Cl + Br, 23·55. $C_{27}H_{46}ClBr$ requires C, 66·75; H, 9·55; Cl + Br, 23·75%). Further elution with light petroleum (100 ml.) afforded 3β-bromo-2α-chlorocholestane (42 mg., 20%) (see below), m. p. and mixed m. p. 150—152°, $[\alpha]_D$ −16° (*c*, 2·01).

(d) *With thionyl chloride*. 2β-Bromocholestan-3α-ol (200 mg.) in pure thionyl chloride (1 ml.) was left at room temperature for 24 hr. The excess of thionyl chloride was removed *in vacuo* and the product chromatographed over alumina (10 g.). Elution with light petroleum (60 ml.) furnished 2β-bromo-3α-chlorocholestane (125 mg., 60%), m. p. and mixed m. p. 130—132°, $[\alpha]_D$ +67° (*c*, 2·90). Further elution with light petroleum (80 ml.) gave 3β-bromo-2α-chlorocholestane (47 mg., 22%) (see below), m. p. and mixed m. p. 149—151°, $[\alpha]_D$ −15° (*c*, 1·34).

Separate quantities of 2β-bromo-3α-chlorocholestane (100 mg.) were treated with phosphorus pentachloride and with thionyl chloride as detailed under (*c*) and (*d*). In both cases an almost quantitative yield of starting material was recovered, identified by m. p., mixed m. p., rotation, and crystal form. No trace of 3β-bromo-2α-chlorocholestane (see below) was produced.

3β-*Bromo*-2α-*chlorocholestane*.—2β-Bromo-3α-chlorocholestane (50 mg.) (see above) was heated under nitrogen at 210—220° for 2 hr. Crystallisation of the product from chloroform–methanol gave 3β-*bromo*-2α-*chlorocholestane* as needles, m. p. 150—152°, $[\alpha]_D$ −16° (*c*, 2·12)

(Found: C, 66·7; H, 9·65; Cl + Br, 23·9. $C_{27}H_{46}ClBr$ requires C, 66·75; H, 9·55; Cl + Br, 23·75%).

Reactions of 2α-Bromocholestan-3β-ol.—This bromohydrin, m. p. 108—112°, $[\alpha]_D$ +12° (*c*, 2·10), was prepared by reduction of 2α-bromocholestan-3-one with sodium borohydride according to the directions of Fieser and Huang (*J. Amer. Chem. Soc.*, 1953, **75**, 4837).

(a) *With hydrobromic acid.* Separate portions (100 mg.) of 2α-bromocholestan-3β-ol were treated with hydrobromic acid at room temperature and at 100° as described above. Chromatography over alumina (4 g.) and elution with 1 : 1 light petroleum–benzene gave 2α-bromocholestan-3β-yl acetate (47% and 54% respectively), m. p. and mixed m. p. 108—111°, $[\alpha]_D$ −8° (*c*, 2·45) and −8° (*c*, 1·96) respectively. The authentic specimen, prepared from the alcohol by pyridine–acetic anhydride (Fieser and Huang, *loc. cit.*), had m. p. 108—111°, $[\alpha]_D$ −8° (*c*, 2·07).

(b) *With phosphorus pentabromide.* 2α-Bromocholestan-3β-ol (200 mg.) was treated with phosphorus pentabromide as described above. The product was chromatographed over alumina (7 g.). Elution with ether (25 ml.) and ether–methanol (50 ml.) gave back unchanged starting material (130 mg., 65%), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +12° (*c*, 2·01)}, and crystal form.

(c) *With phosphorus pentachloride.* 2α-Bromocholestan-3β-ol (200 mg.) was treated with phosphorus pentachloride as described above. The product was chromatographed over alumina (7 g.), but the complex mixture could not be resolved into any component of establishable homogeneity.

(d) *With thionyl chloride.* 2α-Bromocholestan-3β-ol (200 mg.) was treated with thionyl chloride as described above. Chromatography of the total product over alumina (7 g.) and elution with ether (50 ml.) and with 5 : 1 ether–methanol (50 ml.) gave back starting material (136 mg., 68%), identified by m. p., mixed m. p., rotation, {$[\alpha]_D$ +13° (*c*, 1·98)}, and crystal form.

2β-Chlorocholestan-3α-ol.—2α : 3α-Epoxycholestane (1·0 g.) in chloroform (15 ml.) was treated with a stream of hydrogen chloride gas (cf. Barton and Miller, *J. Amer. Chem. Soc.*, 1950, **72**, 370) at room temperature for 5 min. The chloroform solution was washed with water and dilute sodium carbonate solution before being dried (Na_2SO_4) and evaporated *in vacuo*. Crystallisation of the residue from ether–methanol gave 2β-*chlorocholestan*-3α-*ol* as feathery needles, m. p. 118—120°, $[\alpha]_D$ +39° (*c*, 1·84) (Found: C, 76·45, 76·65; H, 10·75, 11·1; Cl, 9·1, 7·0. $C_{27}H_{47}OCl$ requires C, 76·65; H, 11·2; Cl, 8·4%). Acetylation with pyridine–acetic anhydride at room temperature overnight afforded 2β-*chlorocholestan*-3α-*yl acetate*, leaflets (from acetone–methanol), m. p. 128—130°, $[\alpha]_D$ +68° (*c*, 2·04) (Found: C, 75·25; H, 10·55; Cl, 7·6. $C_{29}H_{49}O_2Cl$ requires C, 74·9; H, 10·6; Cl, 7·6%).

2β-Chlorocholestan-3α-ol (176 mg.) in "AnalaR" acetic acid (15 ml.) was treated with chromium trioxide (33 mg.) in the minimum of water at room temperature overnight. Crystallisation from cold acetone–methanol afforded 2β-*chlorocholestan*-3-*one*, m. p. 118—120°, $[\alpha]_D$ +124° (*c*, 2·02) (Found: C, 77·15; H, 10·85; Cl, 8·2. $C_{27}H_{45}OCl$ requires C, 77·0; H, 10·75; Cl, 8·4%). This ketone (50 mg.) in "AnalaR" acetic acid (10 ml.) was treated under reflux with zinc (700 mg.) for 14 hr. The product (Beilstein test negative) was identified as cholestan-3-one by m. p., mixed m. p., and rotation {$[\alpha]_D$ +41° (*c*, 1·98)}.

Reactions of 2β-Chlorocholestan-3α-ol.—(a) *With hydrobromic acid.* 2β-Chlorocholestan-3α-ol (100 mg.) was treated with 50% hydrobromic acid at room temperature as described above. Chromatography of the total product over alumina (3 g.) and elution with light petroleum (100 ml.) and 1 : 1 light petroleum–benzene (100 ml.) gave 2β-chlorocholestan-3α-yl acetate (77 mg., 70%) identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +70° (*c*, 2·11)}, and crystal form.

(b) *With phosphorus pentachloride.* 2β-Chlorocholestan-3α-ol (200 mg.) was treated with phosphorus pentachloride as described above. Chromatography over alumina (7 g.) and elution with light petroleum (60 ml.) gave 2β : 3α-dichlorocholestane (129 mg., 62%), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +62° (*c*, 1·90)}, and crystal form. Further elution with light petroleum (80 ml.) afforded 2α : 3β-dichlorocholestane (35 mg., 17%), identified likewise {$[\alpha]_D$ −6° (*c*, 1·82)}.

Reactions of 2α-Chlorocholestan-3β-ol.—This chlorohydrin, m. p. 115—118°, $[\alpha]_D$ +15° (*c*, 2·14), was prepared from 2α-chlorocholestanone by sodium borohydride, according to the directions of Beereboom, Djerassi, Ginsburg, and Fieser (*J. Amer. Chem. Soc.*, 1953, **75**, 3500).

(a) *With hydrobromic acid.* 2α-Chlorocholestan-3β-ol (100 mg.) was treated with 50% hydrobromic acid at room temperature as detailed above. Chromatography over alumina

(3 g.) and elution with light petroleum (60 ml.) and with 1 : 1 light petroleum–benzene (80 ml.) gave 2α-chlorocholestan-3β-yl acetate (91 mg., 80%), m. p. 122—124° (from acetone–methanol), $[\alpha]_D$ −5° (*c*, 2·78), undepressed in m. p. on admixture with an authentic specimen, m. p. 122—124°, $[\alpha]_D$ −5° (*c*, 2·32) (Beereboom *et al.*, *loc. cit.*).

(b) *With thionyl chloride.* 2α-Chlorocholestan-3β-ol (100 mg.) was treated with thionyl chloride as described above. Chromatogaphy of the product over alumina (3 g.) and elution with 1 : 1 benzene–ether (100 ml.) gave back starting material (75 mg., 75%), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +15° (*c*, 2·20)}, and crystal form.

(c) *With phosphorus pentachloride.* The same results were obtained as with 2α-bromocholestan-3β-ol (see above).

2β : 3β-*Epoxycholestane.*—The following method was convenient for relatively large-scale preparations. 2α-Bromocholestan-3β-ol (Fieser and Huang, *loc. cit.*) (2·0 g.) in ether (10 ml.) and *iso*propanol (25 ml.) was treated with *iso*propanolic potassium hydroxide (4%; 100 ml.) at 55—60° for 1½ hr. Two crystallisations of the product from ether–methanol gave pure 2β : 3β-epoxycholestane (1·0 g.), needles, m. p. 89—91°, $[\alpha]_D$ +56° (*c*, 2·17). The epoxide was reduced with lithium aluminium hydride according to the directions of Fürst and Plattner (*Helv. Chim. Acta*, 1949, **32**, 275), to give cholestan-2β-ol, m. p. 152—154°, $[\alpha]_D$ +34° (*c*, 2·36). Chromic acid oxidation in the usual way gave cholestan-2-one, m. p. 128—130°, $[\alpha]_D$ +50° (*c*, 2·03).

3α-*Bromocholestan*-2β-*ol.*—2β : 3β-Epoxycholestane (1·0 g.) was treated with aqueous hydrobromic acid as for the corresponding α-epoxide (see above). Crystallisation of the product from cold ether–methanol gave 3α-*bromocholestan*-2β-*ol* as plates, m. p. 133—135°, $[\alpha]_D$ +62° (*c*, 2·22) (Found: C, 69·8, 68·7; H, 10·0, 10·3; Br, 16·8. $C_{27}H_{47}OBr$ requires C, 69·35; H, 10·1; Br, 17·1%). Acetylation with pyridine–acetic anhydride overnight at room temperature afforded 3α-*bromocholestan*-2β-*yl acetate*, blades (from acetone–methanol), m. p. 124—126°, $[\alpha]_D$ +72° (*c*, 1·66) (Found: C, 68·9, 68·6; H, 9·6, 10·05; Br, 16·05. $C_{29}H_{49}O_2Br$ requires C, 68·35; H, 9·7; Br, 15·7%).

3α-Bromocholestan-2β-ol (110 mg.) in "AnalaR" acetic acid (10 ml.) was treated with chromium trioxide (19 mg.) in the minimum of water at room temperature overnight. Crystallisation of the product (precipitated during the oxidation) from chloroform–methanol gave 3α-*bromocholestan*-2-*one* as needles, m. p. 151—153°, $[\alpha]_D$ +184° (*c*, 2·38) (Found: C, 69·4; H, 9·6; Br, 17·35. $C_{27}H_{45}OBr$ requires C, 69·65; H, 9·75; Br, 17·15%). This bromo-ketone (40 mg.) in "AnalaR" acetic acid (8 ml.) was refluxed with zinc dust (500 mg.) for 4 hr. Crystallisation from methanol gave cholestan-2-one, identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +51° (*c*, 1·17)}, and crystal form.

Reactions of 3α-*Bromocholestan*-2β-*ol.*—(a) *With hydrobromic acid.* 3α-Bromocholestan-2β-ol (200 mg.) was treated with 50% hydrobromic acid at room temperature as described above. The product was chromatographed over alumina (7 g.). Elution with light petroleum (50 ml.) gave 2β : 3α-dibromocholestane (150 mg., 66%), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +76° (*c*, 2·16)}, and crystal form. Further elution with light petroleum (50 ml.) afforded 2α : 3β-dibromocholestane (15 mg.; 7%), identified likewise {$[\alpha]_D$ −27° (*c*, 0·55)}.

(b) *With phosphorus pentachloride.* 3α-Bromocholestan-2β-ol (200 ml.) was treated with phosphorus pentachloride as detailed above. The product was chromatographed over alumina (7 g.). Elution with light petroleum (50 ml.) gave 3α-*bromo*-2β-*chlorocholestane* (160 mg., 77%), needles or blades (from ethyl acetate–methanol), m. p. 90—92°, $[\alpha]_D$ +62° (*c*, 1·89) (Found: C, 66·7; H, 9·65; Cl + Br, 23·5. $C_{27}H_{46}ClBr$ requires C, 66·75; H, 9·55; Cl + Br, 23·75%). Further elution with light petroleum (50 ml.) afforded 2α-bromo-3β-chlorocholestane (16 mg., 8%) (see below) identified by m. p., mixed m. p., rotation {$[\alpha]_D$ −17° (*c*, 1·06)}, and crystal form.

(c) *With thionyl chloride.* 3α-Bromocholestan-2β-ol (200 mg.) was treated with thionyl chloride as detailed above. The product was chromatographed over alumina (7 g.). Elution with light petroleum (50 mg.) gave 3α-bromo-2β-chlorocholestane (150 mg., 72%), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +61° (*c*, 1·95)}, and crystal form. Further elution with light petroleum afforded 2α-bromo-3β-chlorocholestane (14 mg., 7%) (see below), identified in the same way {$[\alpha]_D$ −16° (*c*, 0·88)}.

2α-*Bromo*-3β-*chlorocholestane.*—3α-Bromo-2β-chlorocholestane (see above) (50 mg.) was heated under nitrogen at 200—210° for 3 hr. Crystallisation of the product from chloroform–methanol furnished 2α-*bromo*-3β-*chlorocholestane* as needles, m. p. 134—136°, $[\alpha]_D$ −17° (*c*, 2·34) (Found: C, 66·7; H, 9·8; Cl + Br, 23·5. $C_{27}H_{46}ClBr$ requires C, 66·75; H, 9·55; Cl + Br, 23·75%).

3α-*Chlorocholestan*-2β-*ol.*—2β : 3β-Epoxycholestane (1·0 g.) was treated with hydrogen chloride as detailed above. Crystallisation of the product from ether–methanol gave 3α-*chloro*-

cholestan-2β-ol as blades, m. p. 109—111°, $[\alpha]_D$ +53° (*c*, 2·34) (Found: C, 76·1, 77·1; H, 11·2, 11·2; Cl, 8·9. $C_{27}H_{47}OCl$ requires C, 76·65; H, 11·2; Cl, 8·4%). Acetylation with pyridine–acetic anhydride at room temperature overnight gave 3α-chlorocholestan-2β-yl acetate (see above), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +62° (*c*, 2·20)}, and crystal form.

3α-Chlorocholestan-2β-ol (104 mg.) in "AnalaR" acetic acid (10 ml.) was treated with chromium trioxide (20 mg.) in the minimum of water at room temperature overnight. The product, which was precipitated during the reaction, was crystallised from chloroform–methanol to give 3α-*chlorocholestan-2-one* as needles, m. p. 162—164°, $[\alpha]_D$ +160° (*c*, 2·40) (Found: C, 76·85; H, 10·65; Cl, 8·8. $C_{27}H_{45}OCl$ requires C, 77·0; H, 10·75; Cl, 8·4%). This chloro-ketone (50 mg.) in "AnalaR" acetic acid (10 ml.) was heated under reflux with zinc (700 mg.) for 14 hr. Crystallisation of the product from chloroform–methanol gave cholestan-2-one, identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +50° (*c*, 2·03)}, and crystal form.

Reactions of 3α-*Chlorocholestan*-2β-*ol*.—(a) *With hydrobromic acid*. 3α-Chlorocholestan-2β-ol (100 mg.) was treated with hydrobromic acid at room temperature as detailed above. The product was chromatographed over alumina (3 g.). Elution with light petroleum (60 ml.) and with 1 : 1 light petroleum–benzene (50 ml.) gave 3α-chlorocholestan-2β-yl acetate (84 mg., 73%), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +62° (*c*, 2·07)}, and crystal form.

(b) *With phosphorus pentachloride*. 3α-Chlorocholestan-2β-ol (200 mg.) was treated with phosphorus pentachloride as detailed above. The product was chromatographed over alumina (7 g.). Elution with light petroleum (50 ml.) gave 2β : 3α-dichlorocholestane (150 mg., 78%), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +60° (*c*, 2·24)}, and crystal form. Further elution with light petroleum (60 ml.) afforded 2α : 3β-dichlorocholestane (12 mg., 6%), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ −7° (*c*, 0·61)}, and crystal form.

Bromination of Cholest-3-*ene*.—Cholest-3-ene (185 mg.), m. p. 74—75°, $[\alpha]_D$ +55° (*c*, 2·17), prepared according to Barton and Rosenfelder's method (*loc. cit.*), in carbon tetrachloride (2 ml.) was titrated with a solution of bromine in the same solvent (40 mg. per ml.) during 1 hr. Uptake of bromine corresponded to 1·15 mols. After removal of the carbon tetrachloride *in vacuo* the total product was chromatographed over alumina (7 g.). Elution with light petroleum (50 ml.) gave 3α : 4β-dibromocholestane (210 mg., 79%) as needles (from ethyl acetate–methanol), m. p. 124—126°, $[\alpha]_D$ +5° (*c*, 2·36), undepressed in m. p. on admixture with the cholest-3-ene dibromide of Barton and Rosenfelder (*loc. cit.*). Further elution with light petroleum (50 ml.) afforded 3β : 4α-dibromocholestane (6 mg., 2%), identified (see below) by m. p., mixed m. p., rotation {$[\alpha]_D$ +33° (*c*, 0·54)}, and crystal form.

3β : 4α-*Dibromocholestane*.—3α : 4β-Dibromocholestane (100 mg.) (see above) was heated under nitrogen at 180—190° for 3 hr. Crystallisation of the product from chloroform–methanol afforded 3β : 4α-*dibromocholestane* as needles, m. p. 171—173°, $[\alpha]_D$ +36° (*c*, 2·21) (Found: C, 61·5; H, 8·95; Br, 29·9. $C_{27}H_{46}Br_2$ requires C, 61·15; H, 8·75; Br, 30·15%). 3β : 4α-Dibromocholestane (50 mg.) was smoothly debrominated in refluxing "AnalaR" acetic acid (10 ml.) with zinc dust (500 mg.; added portionwise) for 30 min., to give cholest-3-ene, identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +52° (*c*, 1·82)}, and crystal form.

Tests for Isomorphism.—The following compounds were used: (1) 2β : 3α-dibromo-, (2) 2β : 3α-dichloro-, (3) 2β-bromo-3α-chloro-, (4) 3α-bromo-2β-chloro-, (5) 2α : 3β-dibromo-, (6) 2α : 3β-dichloro-, (7) 3β-bromo-2α-chloro-, and (8) 2α-bromo-3β-chloro-cholestane.

Nos. 1—4 compounds are diaxial, nos. 5—8 diequatorial. The m. p. of a specimen of the lower-melting component of the mixture was always taken at the same time as that of the mixture. Mixed m. p.s were as follows:

Diaxial pairs; no depressions: (1) + (2) 110—115°; (1) + (3) 125—128°; (1) + (4) 100—103°; (2) + (3) 114—119°; (2) + (4) 94—98°; (3) + (4) 110—115°.

Diequatorial pairs; no depressions: (5) + (6) 146—149°; (5) + (7) 146—148°; (5) + (8) 136—140°; (6) + (7) 150—152°; (6) + (8) 138—145°; (7) + (8) 145—150°.

Mixed diequatorial–diaxial pairs; all depressed: (1) + (5) 100—107°; (1) + (6) 110—115°; (1) + (7) 110—114°; (1) + (8) 90—100°; (2) + (5) 104—115°; (2) + (6) 80—90°; (2) + (7) 100—105°; (2) + (8) 85—95°; (3) + (5) 108—112°; (3) + (6) 111—116°; (3) + (7) 112—124°; (3) + (8) 98—105°; (4) + (5) 80—90°; (4) + (6) 85—95°; (4) + (7) 82—95°; (4) + (8) 78—85°.

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