[CONTRIBUTION FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

RELATIONS BETWEEN THE OPTICAL ROTATORY POWER AND STRUCTURE OF POLYNUCLEAR NATURAL PRODUCTS. I. STEROID HYDROCARBONS

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It has long been recognized that optical rotatory power is too complex a phenomenon to permit the quantitative prediction of the optical rotation associated with a given molecular structure to be made by the application of simple empirical methods. Nevertheless the examination of configurationally related asymmetric compounds has led to valuable generalizations, such as van't Hoff's principle of optical superposition, Freudenberg's rule of shift, and Hudson's isorotation rule. In addition, the use of appropriate physical models has made it possible to deduce the optical characteristics of asymmetric molecules and to advance considerable justification for the empirical rules mentioned above.

The steroids provide data pre-eminently suitable for demonstrating the dependence of optical activity upon structure. The work of Callow and Young (1), Bernstein and Wallis (2–4), and Lettré (5) has been consolidated and largely expanded by Barton (6–13), who has made use of Freudenberg's rule of shift as a powerful criterion of homogeneity and structure in the steroid series. His work includes studies of concentration and solvent effects and of the relationship between structure and vicinal effect and a more critical evaluation of data than had heretofore existed.

Barton has treated the data in an empirical manner, but their abundance and nature invite a more general treatment which will associate with them the entire problem of optical activity and molecular asymmetry. The steroid series lends itself to such a treatment; its fused ring skeleton, particularly that of the 5-allo series, is relatively rigid so that ambiguity due to free rotation appears only in the sidechain; the nucleus is largely planar and possesses considerable symmetry; many compounds are known for which good physical and chemical evidence exists for the configuration (relative to the sugars) of every center of asymmetry; and the series is rich in epimeric forms. The purpose of this and subsequent papers is to correlate structural features of steroid molecules by employing theoretical considerations, such as those contained in Kauzmann, Walter, and Eyring's review (14) and empirical rules including those mentioned above and Marker's tabulation (15).

I. SIDECHAIN CENTERS OF ASYMMETRY

van't Hoff suggested that in a molecule containing several asymmetric centers each center contributes independently of the rest (16). This rule is observed to be obeyed in the aliphatic series only when the centers of asymmetry are too far apart to exert a vicinal influence upon each other. Among sterols this con-

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dition is satisfied for substituents at C-24 in the sidechain. Replacement of hydrogen at C-24 by a methyl or an ethyl group creates a new center of asymmetry. Several pairs of C-24 epimers, formally derived from cholesterol, are known (17). Table I shows the rotations[2] of one pair of such isomers, in which the contribution of the 24-methyl group is represented by B, and the optical activity associated with the nuclear centers and C-20 by A. van't Hoff's rule applies here because A and B are separated by two methylene groups.

As expected, the value for A is equal, well within the limits of experimental error, to the molecular rotation of cholestanol. It is also no coincidence that the value for B is approximately equal to the molecular rotation of D-methylethylisopropylmethane, +28° (18).

TABLE I

COMPARISON OF THE MOLECULAR ROTATIONS OF 24-METHYL- AND 24-ETHYLCHOLESTANOLS

STEROL	M_D
Campestanol (24-a-methylcholestanol)	+125° = A + B
Ergostanol (24-b-methylcholestanol)	+64° = A − B
Cholestanol	+93°
A = +94.5°; B = +30.5°	
Poriferastanol (24-a-ethylcholestanol)	+90° = A + B
Stigmastanol (24-b-ethylcholestanol)	+100° = A − B
Cholestanol	+93°
A = +95°; B = −5°	

The alteration of optical rotation incident upon structural modifications of the sidechain can be interpreted in terms of the one-electron theory of optical activity (14), which attributes rotation of the plane of polarized light to the asymmetric action of vicinal groups upon chromophores. Each radical attached to a center of asymmetry is in turn treated as the chromophore, the other three radicals being the vicinal groups. The largest contributions to the optical activity of a molecule are due to the interaction between a chromophore and its vicinal groups taken one at a time (first order effects), but when free rotation is possible a mirror image conformation will exist among the aggregate of molecules for every given conformation. Such interactions will largely cancel out when summed over all conformations, leaving the interactions between the chromophores and pairs of vicinal groups (second order effects) as the determining factors.

Marker (15) has condensed a mass of data on asymmetric trisubstituted methanes into a table, in which each of twenty-nine radicals is assigned an ordinal number by means of which about twenty-two thousand optically active trisubstituted methanes can be related configurationally to the sugar series. Radicals which in Marker's list have low ordinal numbers are characterized by the absence of strong dipoles and labile electrons near the center of asymmetry, while those which have high ordinal numbers all possess these features. Using

[2] All rotations of steroids referred to in this paper were measured in chloroform for the Na_D line.

the term *chromophore* in the sense of Kauzmann, Walter, and Eyring, it can be stated that the radicals in Marker's table are arranged in the order of chromophoric power.

Experimental evidence indicates that a polarizable group separated from the center of asymmetry by several methylene groups is usually too far distant to participate in asymmetric interaction. This is the basis of Tschugaeff's rule (19, 20), which states that the molecular rotations of the members of a series of optically active compounds of the type $Cr_1r_2r_3R$, in which R represents the radicals of an homologous series, approach a limiting value as R increases in size; in other words, that a constant chromophoric value is associated with a chain of several methylene groups. It also follows from the above discussion that when two groups attached to a center of asymmetry are of almost the same chromophoric power, the asymmetric molecule may be virtually optically inactive, as is D-tuberculostearic acid (10-methyloctadecanoic acid) (21) which has a molecular rotation of $+0.27°$. The same concept explains why Walden (22) obtained an inactive 12-hydroxyoctadecanoic acid as the sole hydrogenation product of the active 12-hydroxy-*cis*-9-octadecenoic (ricinoleic) acid. The center of asymmetry of the hydrogenated acid carries two chains of at least five methylene groups, and it is therefore virtually inactive, its optical rotation apparently lying below the threshold of observability. Since the structural peculiarity is a sufficient cause for the apparently anomalous inactivity of the hydrogenated acid, it is unnecessary to suggest mechanisms involving racemization, as has been done by Farkas (23) and by Twigg (24).

The comparison made earlier in this paper of the partial rotations ($\pm 30.5°$) associated with the epimeric C-24 methyl groups with the molecular rotation of D-methylethylisopropylmethane ($+28°$) suggests that the saturated sterol molecule up through C-23 has nearly the same chromophoric value as the ethyl radical. In agreement with this the two epimeric C-24-ethylcholestanols, poriferastanol and stigmastanol (17) are found to have nearly the same rotation, as shown in Table I. In this case also the value for A is almost equal to the molecular rotation of cholestanol.

Cleavage of the sidechains of related C-24 epimers gives products in which the former C-24 atom represents the only asymmetric center. It was first pointed out by Bergmann and Low (17) that on the basis of Marker's table and Freudenberg's rule several of the corresponding methyl and ethyl derivatives whose rotations are of opposite sign must be regarded as having the same absolute configuration. The partial rotations of the C-24 centers of the sterols show the same reversal; B (methyl) $+30°$; B (ethyl) $-5°$.

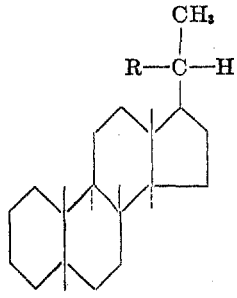
It has been established on the basis of sidechain degradations that most naturally occurring sterols and bile acids have the same configuration with respect to the C-20 methyl group. Bergmann, Feeney, and Swift (25) have already pointed out that there exists a close similarity between the asymmetric centers at C-20 in sterols and bile acids and the center at C-24 in campestanol and ergostanol. Both centers are surrounded by a hydrogen atom, a methyl group, a secondary carbon atom, and a chain of two methylene groups. One might

therefore assume *a priori* that the magnitude of the rotation associated with the center at C-20 is of the same order as that of C-24, *i.e.* that it is $\pm 30°$ rather than $\pm 5°$ as assumed by Fieser (26).

In Table II the molecular rotations of a series of configurationally related steroids, obtained by substituting a C-20 hydrogen of pregnane by a sidechain, are compared with those of the corresponding homogenous trisubstituted methanes (18). In each case the contribution of C-20 is approximated by subtracting the molecular rotation of pregnane (+58°) from the total rotation.

TABLE II

COMPARISON OF THE MOLECULAR ROTATIONS OF C-20 SUBSTITUTED PREGNANES WITH TRISUBSTITUTED METHANES



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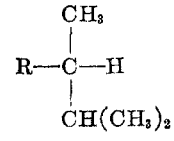

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R	[M]D OF I	[M]D OF I −58°	[M]D OF II	MARKER'S NUMBER
H	+58°	0°	—	—
$(CH_2)_3CH(CH_3)_2$	+97°	+39°	+28°	(9)*
$(CH_2)_2COOH$	+79°	+21°	+17°	5
CH_2COOH	+84°	+26°	+17°	19
COOH	+12°	−46°	+22°	25

* An approximate value: Marker has assigned the ordinal number 9 to the isopentyl group.

The data show that the introduction of the isohexyl group has brought about a change of +39°, the expected approximate value. Unfortunately, rotation data are lacking for isopropylisohexylmethane, but the corresponding methylethylisopropylmethane has a molecular rotation of +28°. On the basis of Tschugaeff's rule and Marker's data, the molecular rotation of the isohexyl derivative is expected to be somewhat higher, approximately +30°.

If the sidechain is shortened and terminated by a carboxyl group, as in cholanic and norcholanic acid, the R- groups have "chromophoric" values and Marker's ordinal numbers approaching that of an isopropyl group (ordinal number 22) or of a tertiary carbon atom. The asymmetric C-20 atom, as it becomes surrounded by more and more nearly equivalent "chromophoric groups," will contribute less and less to the total rotation. This is shown in Table II by the data for cholanic and norcholanic acid. The contribution in these cases has been

reduced to an average of +24°, which is in reasonably good agreement with the average value, +17°, for the corresponding substituted methanes.

Setting aside the anomalous rotation of bisnorcholanic acid, which will be discussed below, the numerical correspondences and the adherence to Freudenberg's rule of shift (27) observed in the two series proves that the configuration at C-20 in most steroids is the same as that at C-24 in campestanol when the tertiary C-17 is equated with an isopropyl group.

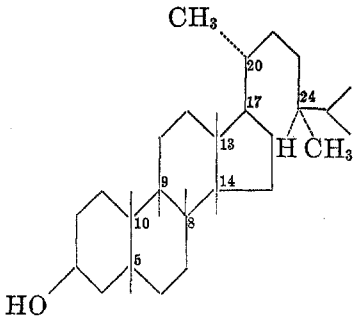
In Table II the molecular rotations of C-20 substituted steroids are compared with that of pregnane, which, however, is not an ideal reference compound. In pregnane, C-17 is attached to a β-oriented, *secondary* C-20 atom, while in the derivatives it is joined to a β-oriented *tertiary* C-20 atom. Some differences in vicinal action are therefore to be expected. In the absence of a more suitable reference compound such as 20-methylpregnane it is advisable to use for comparison methyl norcholanate ($[M]_D$ +70°) and methyl 20-isonorcholanate ($[M]_D$ +60°). This pair of isomers differs only in the configuration at C-20, and an inversion at this center is accompanied by the small change of ±10° in rotation. From this one might conclude that the contribution of C-20 is approximately ±5°, a value which has been adopted by Fieser (26). The small size of this contribution is, however, to be expected, since, as has been shown above, the "chromophoric" value of the $-CH_2COOCH_3$ group is approaching that of a tertiary carbon atom, so that the effective asymmetry at C-20 is low in this particular case. It should be kept in mind that the value for the partial rotation at C-20 is not a constant one but is dependent on the nature of the sidechain. The assignment to C-20 of cholestane of a contribution derived from methyl norcholanate (+5°) is therefore not permissible.

The mean value for the molecular rotations of methyl nor- and 20-isonorcholanate is +65°, and it is this value which most closely corresponds to the approximate partial rotation of an etiocholane nucleus substituted at C-17 by a β-oriented *tertiary* carbon atom. When this value is used in Table II in place of +58° (pregnane), the agreement between the molecular rotations of analogously substituted methanes and pregnanes becomes closer. Thus the difference between coprostane ($[M]_D$ +97°) and +65° is +32°, which is in very good agreement with the expected value for C-20.

The entire sidechain is known to be β-oriented and hindered, so that a carboxyl group attached to C-20 is constrained to occupy a relatively fixed position with respect to the centers of asymmetry at C-13, C-14, and C-17. Due to the lack of free rotation, first order interactions become more important and are sufficient to account for the anomalous optical behavior of bisnorcholanic acid. Fieser (28, 29) and Klyne and Barton (13) have reached the same conclusion as to the configuration at C-20 from independent optical evidence.

The configurations of the asymmetric centers in the sidechain have been arrived at by making use of Marker's table, which in turn is based on Fischer's convention for writing asymmetric structures. Evidence, however, has been advanced by Lardon, Reichstein, and Bergström (30–33) which shows that the present convention for writing steroid ring structures is the reverse of Fischer's

convention. Consistency therefore requires that the sidechain centers of asymmetry also be written reversed. This leads to structure I for campestanol, in which C-21 has been turned back as far as it will go and where the methyl group and the hydrogen at C-24 are viewed as projecting into the paper. If C-16 and C-24 were joined, a structure would result in which both methyl groups in the side-



I

chain would be α-oriented. In corresponding structures for egrostanol the C-24 methyl group would be β-oriented, and for the recently described haliclonasterol (25) the C-24 methyl group would be α-oriented and the C-20 methyl group, β-oriented.

When a double bond is introduced into the 22,23-position of the sidechain, the partial rotation at C-24 is exalted by about $\pm 14°$ in the C-24 methyl series, but is practically unchanged, if not reversed in direction, in the C-24 ethyl series. This is consistent with Levene's data for aliphatic compounds, according to which the RCH=CH- group in substituted methanes would be expected to have an ordinal number between that of an isopropyl and a methyl group (34). Like the carboxyl group, a vinyl group vicinal to C-20 is associated with a negative increment. The average value for A, $-210°$ (See Table III) is lower by $-59°$ than that of cholesterol. In the absence of first order vicinal action a small positive increment ($+15°$) would be expected.

II. NUCLEAR CENTERS OF ASYMMETRY

Strict rotatory additivity is not observed among aliphatic diastereoisomers with vicinal centers of asymmetry presumably because differences in intramolecular repulsions cause each diastereoisomer to assume a different shape characterized by a different set of vicinal actions (14). In cyclic compounds, however, such as the sugars and the menthylamines (35) optical superposition is observed because the atoms of the ring skeleton are more or less constrained to lie in one plane (14). Since fused alicyclic rings cannot be quite planar, strict optical superposition cannot be expected in the steroid ring system, so that the concept of partial rotations associated with nuclear centers of asymmetry is a somewhat tenuous one. Nevertheless, the assumption appears permissible that in a pair of steroids, epimeric at a single center, the partial rotation for this center is approximately half of the difference between the molecular rotations of the epimers.

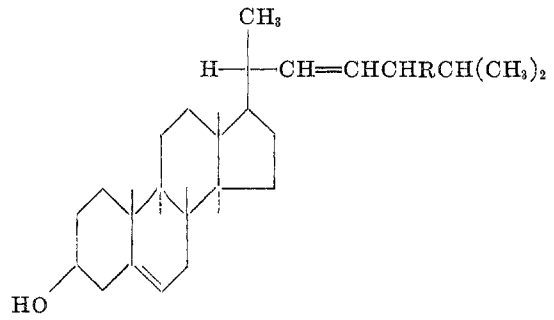
In evaluating these partial rotations it is advisable to use data derived from

saturated hydrocarbons only, or at least to exclude data of compounds possessing "chromophoric" groups, such as hydroxyls or double bonds, near the epimeric center. It should also be borne in mind that the sidechain at C-17 is a substituent which will alter the partial rotations at adjacent centers, such as C-13. The values presented in Table IV parallel those reported by Fieser (36). They are based on additional arguments and on data which had not been available to him.

Fieser (36) has suggested that the biosynthesis of steroids is controlled by a tendency for asymmetric centers to unite in such a manner as to produce a balanced, or neutralized, chain of alternate *dextro-* and *levo*-rotatory centers with three large partial rotations in the center of the chain. It seems, however, more

TABLE III

COMPARISON OF MOLECULAR ROTATIONS OF Δ^{22}-STEROLS



R	[M]D	
a-CH_3	$-168° = A + B$	$A = -212°$; $B = +44°$
b-CH_3	$-256° = A - B$	
a-C_2H_5	$-203° = A + B'$	$A = -207°$; $B' = +4°$
b-C_2H_5	$-211° = A - B'$	
Cholesterol	$-151°$	

reasonable to assume that any alternation in the direction of partial rotation is either fortuitous or more likely due to the alternation of the α- and β-configuration through the planar molecule. The low rotations associated with the centers of ring A are due to its relative symmetry and lack of strain while the high rotation at C-14 is a reflection of the asymmetry caused by the strained fusion of rings C and D.

III. UNSATURATION AT NUCLEAR CENTERS

One of the first relationships between optical activity and structure observed by steroid chemists is the influence exerted by a 4:5 and a 5:6 double bond upon the direction of rotations. The former confers a strong *dextro*-rotation upon the steroid, and the latter a still more pronounced *levo*-rotation. Fieser (36) has stated that no theoretical interpretations have been advanced for these phenomena and that "in each case the asymmetry at C_5 is destroyed and the

TABLE IV

Partial Rotations

CENTER	α-SERIES	$[M]_D^\circ$	REF.	β-SERIES	$[M]_D^\circ$	REF.	$\pm\frac{1}{2}([M]_D^\alpha - [M]_D^\beta)$	FIESER'S VALUE (36)	REMARK
C-5	Cholestane	+91	(10)	Coprostane	+97	(10)	−3 (α)	−10 (α)	Note I
	Androstane	+5	(10)	Etiocholane	+11	(10)	−3 (α)		
	5-Allopregnane	+52	(10)	Pregnane	+58	(10)	−3 (α)		
C-9	Ergostanyl acetate	+27	(36)	Perhydroisopyrocalciferyl acetate	−28	(36)	−27 (α)	−5 (α)	Note I
C-10	Lumistanol	+38	(36)	Ergostanol	+64	(36)	−13 (α)	−5 (α)	Note I
C-8	—	—	—	—	—	—	+25.5 in cholestane	+90 (β)	
C-13	—	—	—	—	—	—		+90 (β)	Note II
C-8	—	—	—	—	—	—	+53 in androstane		Note II
C-13	—	—	—	—	—	—			
C-14	17-Iso-5-allopregnane	−101	(10)	14-Iso-17-iso-5-allopregnane	+72	(10)	−85 (α)	−110 (α)	Note III
C-17	17-Iso-5-allopregnane	−101	(10)	5-Allopregnane	+52	(10)	+76.5 (β) in pregnane		Note IV
C-17	—	—	—	—	—	—	+83.5 (β) in cholestane	+35 (β)	Note IV

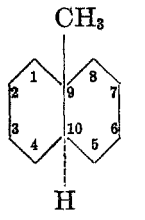
Note I. From a comparison of the values for C-5, C-9, and C-10 the following generalization may be derived: The more symmetrical the surroundings of an asymmetric center the smaller the partial rotation associated with it. Thus C-5, symmetrically surrounded by the quaternary C-10 and two $-(CH_2)_2-$ groups shows the smallest partial rotation, and C-9, asymmetrically surrounded by a quaternary, a tertiary, and a secondary carbon atom, shows the highest. (See Figure I).

Note II. Since Fieser's value for C-8 in cholestane has been derived from data for the highly unsaturated epimers estrone and 8-iso-estrone, it does not appear to be a useful one. In cholestane C-8 has surroundings reminiscent in symmetry of those of C-10 and one might therefore expect its partial rotation to be similarly small. Since rotational data for saturated steroids, epimeric at C-8 and C-13, are unavailable, only the sum of the partial contributions of these centers may be arrived at by subtracting the sum of other partial rotations from the molecular rotation of androstane and cholestane. The partial rotation of C-13 is influenced by a substituent at C-17 and is different in androstane and allopregnane. Table V [see also Klyne (37)] shows that the mean value for the rotations of 17-iso-5-allopregnane and 5-allopregnane differ by about −30° from the molecular rotation of androstane, a difference which represents the influence of the sidechain on C-13.

Note III. Although C-14 has surroundings similar to those of C-9, its partial rotation is larger, illustrative probably of its position at the strained *trans*-junction of rings C and D.

Note IV. As noted elsewhere the magnitude of the contribution of C-17 is dependent on the presence of a secondary or a tertiary carbon atom at this point.

double bond is in a position favorable for strong exaltation of the rotational contribution of carbon atom 10, and yet the pronounced effects are of opposite sign". Actually, the solution to this problem had been advanced years before by Callow and Young (1) with their suggestion that the opposed rotations of Δ^4 and Δ^5-cholestene derivatives are due to the diastereoisomeric arrangement of the carbon atoms around C-5. The situation is best illustrated by regarding cholestane and the two cholestenes as derivatives of the analogous 9-methyldecalin and 9-methyloctalins. The saturated hydrocarbon (II) is optically inactive, but the introduction of a double bond in any position of the molecule gives a racemic derivative. One such pair, D- and L-9-methyl-$\Delta^{4(10)}$-octalin is represented by III and IV. The rigidity of these molecules favors first order interactions which would be expected to confer optical activities of substantial magnitude and opposite sign on III and IV. The molecular rotations of Δ^4- and Δ^5-cholestene (VI and VII) are in accord with this expectation, and the objection that the interaction between the double bond and rings C and D is sufficiently great to vitiate the analogy can be met both on theoretical and experimental grounds.



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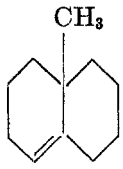

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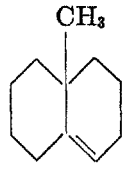

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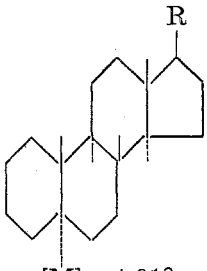
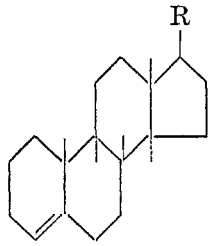


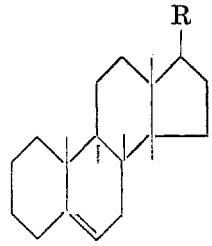
$[M]_D$ +91°

V



$[M]_D$ +248°
Δ +157°

VI



$[M]_D$ −207°
Δ −298°

VII

As has been pointed out by Kirkwood, in the absence of structural resonance the spectrum of an organic group "retains to a large extent its identity in different compounds of which it is a constituent and is influenced considerably only by groups which are its nearest neighbors" (38). Since the major portion of the rotatory power of the above cholestenes is due to an absorption band produced by an asymmetric transition localized in the double bond, the sign and magnitude of this portion of the rotation is influenced only by adjacent atoms near

enough to be appreciably overlapped by the electronic cloud of the double bond's excited state. Experimental evidence presented in Table VI shows that the vicinal action between an asymmetric center and a double bond decreases rapidly with increasing separation and practically vanishes when the distance approaches 4 Å.

The values in Table VI are those which Barton and Klyne obtained by averaging the rotational differences of several comparable pairs of saturated and unsaturated steroids (10). Two series (the 5-normal and the 5-allo) are represented which differ only in the configuration at C-5. In the absence of significant vicinal action between the double bonds, listed in the table, and the atoms surrounding C-5, the Δ values should be about the same and the unsigned second

TABLE V

COMPARISON OF MOLECULAR ROTATIONS OF THE ALLOPREGNANES WITH ANDROSTANE

	$[M]_D$	
17-Iso-5-allopregnane	$-101° = A - B$	$A = -24.5°; B = +76.5°$
5-Allopregnane	$+52° = A + B$	
Androstane	$+5°$	

TABLE VI

VICINAL ACTION BETWEEN C-5 AND DOUBLE BONDS

POSITION OF DOUBLE BOND	($[M]_D$ UNSAT. $-[M]_D$ SAT.)		$\overline{\Delta\Delta}$	DISTANCE FROM CENTER OF DOUBLE BOND TO C-5, Å
	5-normal	*5-allo*		
7,8	+119°	−68°	187°	2.9
9,11	+49°	+109°	60°	3.3
8,14	−37°	−16°	21°	3.6

differences $\overline{\Delta\Delta}$ should be close to zero. The fact that the values differ in the two series proves the existence of vicinal action. The magnitude of the $\overline{\Delta\Delta}$ values is an expression of the degree of vicinal action. As the distance between C-5 and the center of the double bond increases, the $\overline{\Delta\Delta}$ values decrease. Conversely, it is therefore to be expected that the atoms constituting rings C and D will not exert a noticeable influence upon a double bond at C-5, because they are separated from it by more than 4 Å.

Steroids with a double bond in ring A and B in positions other than 4:5 and 5:6 may also be regarded as derivatives of D- and L-9-methyloctalins, and as is to be expected of enantiomorphs the differences between their molecular rotations and that of the corresponding saturated compound are of opposite sign.

In the examples listed in Table VII the Δ values for each pair differ substantially in magnitude because rings C and D are now within range of vicinal action which becomes more apparent as the double bond in ring B is shifted toward ring C. In addition a 7:8 double bond eliminates an asymmetric center.

Of special significance is the difference between the rotations of correspondingly

unsaturated 5-allo and 5-normal steroids. Here the determining factor is clearly the configuration at C-5 (See Table VIII). If in Δ^2- and Δ^7-steroids the contribution of C-5 is represented as +A in the allo and −A in the normal series and the contributions of all other centers as B in the case of Δ^2- and as C in the case of the Δ^7-steroids, the values for A are of the same magnitude and of opposite sign as shown in Table VIII. It appears therefore that the contribution of C-5 is in accord with van't Hoff's principle of optical superposition.

The relations between the structure and optical rotatory power of steroids with oxygen functions will be discussed in a later communication.

TABLE VII

UNSATURATED STEROIDS AND CORRESPONDING 9-METHYLOCTALINS

SERIES	POSITION OF DOUBLE BOND	Δ	REF.	PROBABLE CORRESPONDING 4-METHYLOCTALIN
—	4,5	+159°	10	D-$\Delta^{4(10)}$
	5,6	−298°	10	L-$\Delta^{4(10)}$
	3,4	+149°	10	D-*trans*-Δ^3
	6,7	−448°	39	L-*trans*-Δ^3
5-*allo*	2,3	+152°	10	D-*trans*-Δ^2
	7,8	−68°	10	L-*trans*-Δ^2
5-*normal*	2,3	−41°	10	L-*cis*-Δ^2
	7,8	+119°	10	D-*cis*-Δ^2

TABLE VIII

CONTRIBUTION OF C-5 IN "ENANTIOMORPHIC" UNSATURATED STEROIDS

SERIES	POSITION OF DOUBLE BOND		A
5-*allo*	2,3	A + B = 152°	+96.5°
5-*normal*	2,3	−A + B = −41°	
5-*allo*	7,8	A + C = −68°	−93.5°
5-*normal*	7,8	−A + C = +119°	

SUMMARY

1. The relationship between the stereochemistry of the carbon skeletons of steroids and their optical rotatory power has been discussed in terms of a simplified theory of optical activity and of the associated rules of van't Hoff, Freudenberg, Tschugaeff, and Marker.

2. In the light of the above considerations and the correlation by Bergström, Lardon, and Reichstein of the configuration at C-3 in calciferol with the sugar series, structures have been proposed for the sterols in which every asymmetric center has been assigned a configuration in terms of Fischer's convention.

3. The probable partial rotations of C-20, C-24, and most of the nuclear centers have been estimated and the effects of structural changes on these rotations have been discussed.

4. The rotational differences between saturated steroids and their derivatives, mono-unsaturated in ring A or B, have been shown to possess signs, which can be

explained by the derivation of the respective steroids from enantiomorphic 9-methyloctalins.

5. The dependence of the magnitude of the vicinal action between C-5 and a double bond upon the distance between the two groups has been examined and has been used to determine the probable sphere of vicinal action between any asymmetric center and an unsaturated group in rings A and B.

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