213. *The Application of the Method of Molecular Rotation Differences to Steroids. Part I. Naturally Occurring Sterols and their Simple Derivatives.*

By D. H. R. Barton.

The data available in the literature on the optical rotatory powers of naturally occurring sterols and their simple derivatives have been correlated by the Method of Molecular Rotation Differences (Barton and Jones, *J.*, 1944, 659). Fully hydrogenated sterols (stanols) and sterols containing nuclear unsaturation (stenols) are readily differentiated and characterised. The conclusion of Bernstein, Wilson, and Wallis (*J. Org. Chem.*, 1942, **7**, 103) that α- and β-stenol double bonds do not exert vicinal action at the 3 position in the steroid molecule is untenable.

It is suggested, contrary to the currently accepted formulæ, that both α-spinasterol and episterol possess γ- or $\Delta^{7:8}$-unsaturation, that ascosterol and faecosterol both have the nuclear double bond in the C_9—C_{11} position, and that neosterol is impure ergosterol; chemical evidence in favour of these views is advanced.

By this method a number of sterols reported in the literature cannot be assigned to any class; in most cases these aberrations are probably due to impurity, but certain of these steroids are related in molecular rotation differences to the triterpenoids. Examples are provided by the α-sitosterols, the tritisterols, and satisterol. Finally it is shown that there is a well-defined and characteristic differentiation between the molecular rotation differences of sterols and triterpenoids (Table VII) and it is a simple matter to assign one of these substances to its class.

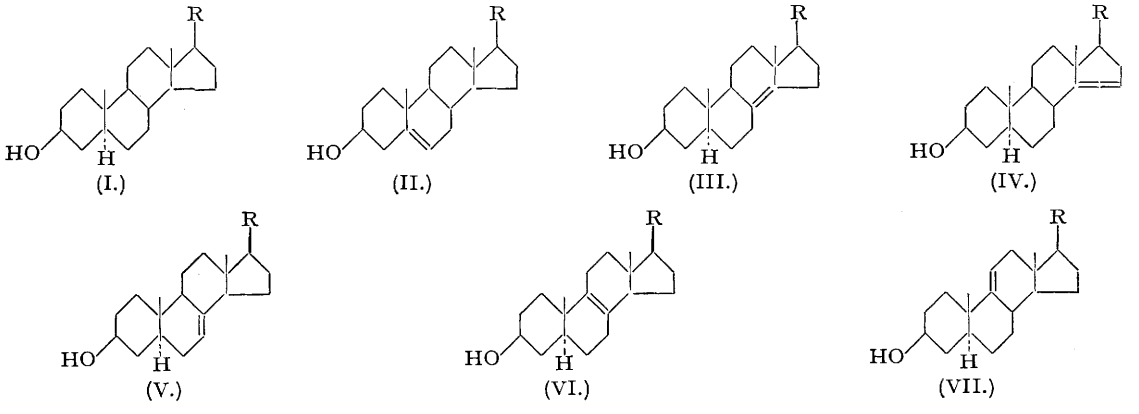
The last decade has seen a remarkable increase in the importance attached to the steroids. This has been due, on the one hand, to the correct formulation of the basic skeletal structure of the group and, on the other, to the physiologically important substances now included in, or closely related to, this class of naturally occurring materials. As the amount of data relating to the optical rotatory power of steroids has grown, there have been attempts to correlate the variation of this physical constant with the known structures of the molecules. The earlier papers of Lettré (*Ber.*, 1937, **70**, 450) and Callow and Strain (*Proc. Roy. Soc.*, 1936, A, **157**, 194) were followed by those of Wallis and his co-workers (*J. Org. Chem.*, 1941, **6**, 319; 1942, **7**, 103), and a number of useful generalisations have been proposed. The latter authors examined the data in the light of modern theories of optical rotatory power (compare Kauzman, Walter, and Eyring, *Chem. Rev.*, 1940, **26**, 339), which suggest that the Principle of Optical Superposition and the Freudenberg " Rule of Shift " (*Ber.*, 1933,

66, 177) would be rigidly obeyed if the groups under consideration were situated sufficiently far apart in space for " vicinal action " to be inoperative. The definition of the distance over which " vicinal action " is effective is obviously of the greatest interest and further reference is made to this subject below. Plattner and Heusser (*Helv. Chim. Acta*, 1944, **27**, 748) have made observations on the dependence of optical rotatory power on structure in certain bile acid derivatives, and have confirmed the finding of Wallis *et al.* (*loc. cit.*) that changes in the steroid side chain do not exert vicinal action at the 3 position.

Recently the relationship between optical rotatory power and structure in triterpenoid compounds has been examined by Barton and Jones (*loc. cit.*) by their " Method of Molecular Rotation Differences." It was shown that triterpenoids are divided thereby into the same groups as those obtained by chemical classification, and that generalisations relating changes in optical rotatory power to alterations in structure could be made. This method is now applied to naturally occurring sterols.

In the tables discussed below all optical rotatory power data refer to the Na_D line with chloroform as solvent, unless specified to the contrary, and are expressed as molecular rotations, the specific rotation data in the literature having been approximated to the nearest degree and averaged. When the values recorded are grossly at variance this is usually pointed out in the text, but some of the older values, which are obviously in error, have been disregarded. The usually permissible error of a specific rotation is of the order ± 2—3° (*i.e.*, about ± 10 in the molecular rotation), but many substances have constants which are known to considerably finer limits than this and, in any case, the permissible error will depend on a number of factors (see Barton and Jones, *loc. cit.*). Δ_1 is the molecular rotation difference (M.R.D.) between the values for the acetate and the sterol, Δ_2 that between the benzoate and the sterol and so on.

In Table I the data for fully hydrogenated sterols (stanols) of the 3(β)-*trans* configuration (I) have been collected, whilst in Table II the corresponding values for Δ^5-unsaturated sterols (stenols) (II) are summarised.



(I.) (II.) (III.) (IV.) (V.) (VI.) (VII.)

A small number of sterols comprising bombicesterol and bombicestanol, the sterol B of Heilbron *et al.* (*J.*, 1941, 344), and its dihydro-derivative, gorgosterol, δ-sitosterol, and microcionasterol have M.R.D.'s which are incompatible with the views expressed as to their nature and with any other reasonably possible structures. It is suggested that all these materials are impure and, indeed, this is acknowledged to be the case with the above-mentioned sterol B, gorgosterol, and microcionasterol.

TABLE I.

Substance.	Formula.	[M]D. *Sterol.*	*Acetate.*	*Benzoate.*	*Ketone.*	*Dinitrobenzoate.*	Δ_1.	Δ_2.	Δ_3.	Δ_4.	References.
Cholestanol	(I; R = C_8H_{17})	+ 93	+ 60	+ 98	+158	—	−33	+ 5	+65	—	1, 2, 3, 4, 5.
Campestanol	(I; R = C_9H_{19})	+125	+ 80	—	—	+131	−45	—	—	+ 6	6.
Ergostanol	(I; R = C_9H_{19})	+ 64	+ 27	—	+140	+ 77	−37	—	+76	+13	7, 8, 9, 10, 11, 12, 13, 14.
Stellastanol	(I; R = C_9H_{19})	+ 88	+ 62	—	—	—	−26	—	—	—	15.
Poriferastanol	(I; R = $C_{10}H_{21}$)	+104	+ 78	—	+186	+104	−26	—	+82	± 0	16, 17.
γ-Sitostanol	(I; R = $C_{10}H_{21}$)	+ 83	+ 46	—	+157	—	−37	—	+74	—	18, 19.
Stigmastanol	(I; R = $C_{10}H_{21}$)	+100	+ 69	+104	+170	+ 85	−31	+ 4	+70	−15	18, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31.
Anomalous :											
Bombicestanol	(I; R = C_8H_{17})	− 43	+ 43	—	—	—	+86	—	—	—	32.
Dihydro-sterol B	(I; R = $C_{10}H_{21}$)	+ 25	− 37	—	—	—	−62	—	—	—	28.
Sterol B	(I; R = $C_{10}H_{19}$)	−107	−128	− 78	—	—	−21	+29	—	—	28.

Both stanols and Δ^5-stenols possess Δ_1 values of about −34, but differ widely and characteristically in their Δ_2 values. In agreement with the view of Bernstein, Wilson, and Wallis (*J. Org. Chem.*, 1942, **7**, 103) and of Kind and Bergmann (*ibid.*, 1942, **7**, 341), Mazur's formulation (*J. Amer. Chem. Soc.*, 1941, **63**, 2442) of spongillasterol as 5 : 6-dihydrostigmasterol appears to be in error, as its Δ_2 value is normal for that expected of a Δ^5-stenol. From the data available it seems that there is little to chose between the M.R.D.'s of benzoates and 3 : 5-dinitrobenzoates in the steroid field.

TABLE II.

Substance.	Formula.	[M]D. Sterol.	Acetate.	Benzoate.	Ketone.*	Dinitrobenzoate.	Δ_1.	Δ_2.	Δ_3.	Δ_4.	References.
24 : 25-Dehydrocholesterol	(II; R = C_8H_{15})	−146	—	− 63	—	—	—	+83	—	—	33.
Cholesterol	(II; R = C_8H_{17})	−151	−184	− 64	+357	− 81	−33	+87	+508	+70	1, 3, 5, 26, 33, 34, 35, 36, 37, 38, 39.
24-Ketocholesterol	(II; R = $C_8H_{15}O$)	−148	−181	—	—	—	−33	—	—	—	40.
Brassicasterol	(II; R = C_9H_{17})	−244	−287	—	—	−167	−43	—	—	+77	22, 41.
Campesterol	(II; R = C_8H_{17})	−132	−159	− 50	—	− 42	−27	+82	—	+90	42.
22 : 23-Dihydrobrassicasterol	(II; R = C_9H_{19})	−184	−203	− 96	—	−101	−19	+88	—	+83	43.
Fucosterol	(II; R = $C_{10}H_{19}$)	−169	−204	− 83	+312	—	−35	+86	+481	—	44, 45, 46, 47, 48.
Poriferasterol	(II; R = $C_{10}H_{19}$)	−206	−241	−114	+235	−133	−35	+92	+441	+73	17, 49.
Stigmasterol	(II; R = $C_{10}H_{19}$)	−202	−241	−129	+246	−133	−39	+73	+448	+69	25, 43, 48, 50, 51, 52, 53, 54.
Clionasterol	(II; R = $C_{10}H_{21}$)	−153	−192	− 88	+330	− 85	−39	+65	+483	+68	16, 17, 55.
β-Sitosterol	(II; R = $C_{10}H_{21}$)	−149	−178	− 73	+354	− 61	−29	+76	+503	+88	21, 26, 28, 43, 51, 52, 56, 57, 58, 59.
γ-Sitosterol	(II; R = $C_{10}H_{21}$)	−178	−210	−104	—	—	−32	+74	—	—	18, 59, 60.
ε-Sitosterol	(II; R = $C_{10}H_{21}$)	−162	−205	—	—	—	−43	—	—	—	52.
Spongillasterol	(II; R = $C_{10}H_{21}$)	−174	−219	− 88	—	−109	−45	+86	—	+65	20.
Anomalous :											
Bombicesterol	(II; R = C_8H_{17})	−124	−188	− 69	—	—	−64	+55	—	—	32.
Gorgosterol	Uncertain	−184	−252	—	—	−240	−68	—	—	−56	35.
Microcionasterol	Uncertain	− 83	−114	− 57	—	—	−31	+26	—	—	61.

* Δ^4-3-Ketones.

TABLE III.

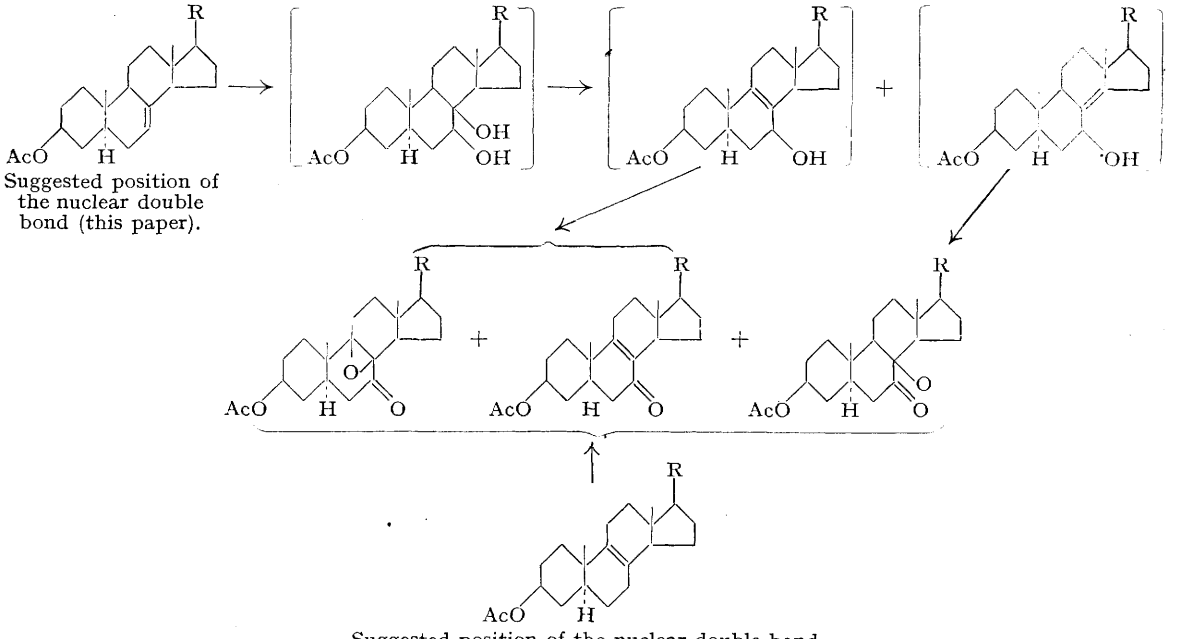
Substance.	Formula.	[M]D. Sterol.	Acetate.	Benzoate.	Ketone.	Δ_1.	Δ_2.	Δ_3.	References.
α- or 8 : 14-Stenols :									
α-Cholestenol	(III; R = C_8H_{17})	+ 81	+ 43	+ 39	—	−38	−42	—	3, 62, 63, 64, 65.
α-Ergostenol	(III; R = C_9H_{19})	+ 48	+ 4	+ 5	+151	−44	−43	+103	66, 67, 68, 69, 70, 71, 72
α-Stellastenol	(III; R = C_9H_{19})	+ 80	+ 57	—	—	−23	—	—	15.
α-Stigmastenol	(III; R = $C_{10}H_{21}$)	+ 99	+ 59	+ 57	—	−40	−42	—	73, 74, 75, 76.
β- or 14 : 15-Stenols :									
β-Zymosterol	(IV; R = C_8H_{15})	+143	—	+152	—	—	+ 9	—	33.
β-Cholestenol	(IV; R = C_8H_{17})	+124	+ 94	+157	—	−30	+33	—	1, 3, 62.
β-Ergostenol	(IV; R = C_9H_{19})	+ 72	+ 31	+101	+147	−41	+29	+ 75	7, 8, 11, 70, 77.
β-Stellastenol	(IV; R = C_9H_{19})	+116	+ 84	—	—	−32	—	—	15.
γ- or 7 : 8-Stenols :									
γ-Cholestenol	(V; R = C_8H_{17})	± 0	± 0	+ 34	—	± 0	+34	—	62.
α-Dihydroergosterol	(V; R = C_9H_{17})	− 80	− 87	− 45	—	− 7	+35	—	66, 78, 79, 80, 81, 82, 83.
γ-Ergostenol	(V; R = C_9H_{19})	+ 4	− 26	+ 10	—	−30	+ 6	—	68, 70, 72, 79, 80.
α-Spinasterol	(V; R = $C_{10}H_{19}$)	− 12	− 23	+ 10	+ 82	−11	+22	+ 94	73, 76, 84, 85.
β-Spinasterol	(V; R = $C_{10}H_{19}$)	+ 25	+ 23	+ 41	—	− 2	+16	—	73.
δ-Spinasterol	(V; R = $C_{10}H_{19}$)	+ 25	+ 5	+ 57	—	−20	+32	—	73.
δ- or 8 : 9-Stenols :									
δ-Cholestenol	(VI; R = C_8H_{17})	+ 45	+ 60	—	—	+15	—	—	63, 80.
ε- or 9 : 11-Stenols :									
Zymosterol	(VII; R = C_8H_{15})	+192	+145	+190	+290	−47	− 2	+ 98	1, 3, 33, 65, 86, 87.
Zymostenol	(VII; R = C_8H_{17})	+193	+137	+201	+277	−56	+ 8	+ 84	1, 33.

Data for α- (III), β- (IV), γ- (V), δ- (VI), and ε- (VII) stenols are correlated in Table III. In connection with what follows below it should be pointed out that the Δ_1 and Δ_2 values for α- and β-cholestenols and ergostenols are especially reliable, as they have been recorded in good agreement with each other on numerous occasions. It would be expected that a comparison of the M.R.D.'s of stenols and stanols would afford some indication of the distance of operation of " vicinal action," for the further the double bond away from the 3-position, the more nearly should the M.R.D.'s of the stenol approach those of the stanol type. In actual fact there is little indication of the occurrence of such a phenomenon in Table III, at least as far as nuclear unsaturation is concerned. The M.R.D.'s observed are seen to be highly dependent upon the position of the double bond, and the statement of Bernstein, Wilson, and Wallis (*loc. cit.*) that α- and β-stenols have the double bond in positions no longer subject to " vicinal action " is untenable. δ-Cholestenol is exceptional in having a positive Δ_1 value; it is necessary that this be confirmed.

There has recently been discussion as to the correct position of the nuclear double bond in α-dihydroergosterol and in α-spinasterol. It has been customary to formulate α-dihydroergosterol, previous to the work mentioned below, as (III; R = C_9H_{17}) and α-spinasterol as (III; R = $C_{10}H_{19}$) or (V; R = $C_{10}H_{19}$) with the γ-position of the double bond for preference (Fernholz and Ruigh, *J. Amer. Chem. Soc.*, 1940, **62**, 2341). The optical rotatory power data (see Table III) definitely preclude the presence of the double bond at the α-position in these two sterols, and critical examination of the available chemical evidence shows the correctness of this deduction.

Stavely and Bollenback (*J. Amer. Chem. Soc.*, 1943, **65**, 1290) oxidised α-dihydroergosterol acetate with chromic acid and isolated products which, they claimed, proved the double bond to be in the δ-position (VI; R = C_9H_{17}). Wieland and Benend (*Annalen*, 1943, **554**, 1), on the other hand, by a comparatively unambiguous method, showed that the nuclear unsaturation must be at the γ-position (V; R = C_9H_{17}). Stavely and Bollenback also (*J. Amer. Chem. Soc.*, 1943, **65**, 1600) oxidised α-spinasterol acetate under the same conditions as for α-dihydroergosterol acetate and claimed that the nature of the oxidation products showed the original

double bond to have occupied the δ-position (VI; R = $C_{10}H_{19}$). The most reasonable explanation of these discrepancies is that the two sterols in question both contain γ-double bonds, and that these rearrange, with the initially formed 7 : 8-diol as intermediate, on chromic acid oxidation.



Suggested position of the nuclear double bond (this paper).

Suggested position of the nuclear double bond (Stavely and Bollenback, *loc. cit.*).

This postulated shift of the double bond explains more easily than the suggestions of Stavely and Bollenback (*loc. cit.*) the nature of the oxidation products of α-dihydroergosterol and α-spinasterol acetates. In any case it is necessary on the δ-ethenoid formulæ for these compounds to postulate a shift from the δ- to the α-position under the influence of chromic acid oxidation in order to account for the occurrence of the 8 : 14-oxido grouping in one of the oxidation products.

In Table III, therefore, α-dihydroergosterol and α-spinasterol have been classified as γ-stenols and their M.R.D.'s agree reasonably well with each other and with those recorded for γ-cholestenol. The specific rotations available in the literature for γ-ergostenol are in marked disagreement with each other and it is not surprising, therefore, that the M.R.D.'s for this substance do not resemble those reported for the other γ-stenols.

In connection with this apparent double bond migration, Eck and Hollingsworth (*J. Amer. Chem. Soc.*, 1941, **63**, 2986) recently claimed to have prepared δ-cholestene by dehydration of 7-hydroxycholestane, proving the identity of their product by chromic acid oxidation to 7-keto-δ-cholestene. Wintersteiner and Moore (*J. Amer. Chem. Soc.*, 1943, **65**, 1507), on the other hand, have shown that on dehydration of 7-(β)-hydroxycholestanyl acetate by the same procedure a mixture of olefinic isomers results in which γ-cholestenyl acetate is strongly predominant. It is likely, therefore, that δ-cholestene has been wrongly described and is, in reality, substantially γ-cholestene, the expected dehydration product. The apparent migration of double bonds under the influence of chromic acid oxidation is not altogether a new concept, as a similar rearrangement has been suggested to occur in triterpenoids (compare Noller, *J. Amer. Chem. Soc.*, 1944, **66**, 1269; Haworth, *Ann. Rep.*, 1937, **34**, 327).

Optical rotatory power is helpful also in considering the position of the nuclear double bond in β- and δ-spinasterols (suitable data for γ-spinasterol are not available). In Table III these sterols have been included with the γ-stenols, to which group they most closely approximate. This classification predicts, therefore, that α-, β-, and δ-spinasterols differ from each other solely in the position of the unsaturated centre in the side chain. It is not possible, however, to exclude entirely δ- or $\Delta^{8:9}$-unsaturation in β- and δ-spinasterols.

It will be noticed from Table III that not only is the position of nuclear unsaturation indicated by M.R.D. values, but that the magnitude of the molecular rotation of the unsubstituted stenol, itself, lies between limits roughly characteristic of the double bond position. Thus Δ^5-stenols have $[M]_D$ lying between −130° and −210°, α-stenols between +50° and +100°, β-stenols between +70° and +140°, γ-stenols between 0° and −80°, and ε-stenols about +190°.

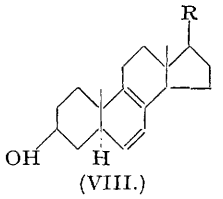
The minor steroid constituents of yeast fat have recently been the subject of renewed interest (Wieland, Rath, and Hesse, *Annalen*, 1941, **548**, 34; compare Wieland and Kanaoka, *Annalen*, 1937, **530**, 146; Wieland and Gough, *Annalen*, 1930, **482**, 36). The molecular rotation data available in the literature for this group of sterols are summarised in Table IV; in this table the data for *iso*-dehydrocholesterol are included for comparative purposes. According to Wieland, Rath, and Hesse (*loc. cit.*), ascosterol is diethenoid, possessing a

TABLE IV.

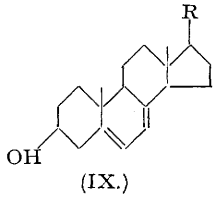
Substance.	Formula : Suggested in literature.	Formula : Suggested in this paper.	$[M]_D$. *Sterol.*	*Acetate.*	*Benzoate.*	Δ_1.	Δ_2.	References.
Ascosterol	(V or VI; R = C_9H_{17})	(VII; R = C_9H_{17})	+179	+ 97	+196	− 82	+ 17	66, 86, 88.
Episterol	(III; R = C_9H_{17})	(V; R = C_9H_{17})	+ 4	− 18	+ 60	− 22	+ 56	66, 89.
Faecosterol	(III; R = C_9H_{17})	(VII; R = C_9H_{17})	+167	+ 88	+176	− 79	+ 9	66, 86.
Neosterol	(VIII; R = C_9H_{17})	(IX; R = C_9H_{17})	−416	−294	−230	+122	+186	66, 86.
*iso*Dehydrocholesterol	(VIII; R = C_8H_{17})	—	− 69	− 47	− 17 *	+ 22	+ 52	63.

* This value is recorded for the dinitrobenzoate; it is unlikely to be far removed from that for the benzoate.

methylene group in the side chain and nuclear unsaturation in the γ- or δ-position. Faecosterol was said to be identical with ascosterol save that the nuclear double bond was in the α-position. Episterol was similarly thought to be identical with faecosterol save that the side chain methylene group was placed in a different position. Neosterol, a triethenoid steroid, was assigned the structure (VIII; R = –CHMe·CH:CH·CHMe·$CHMe_2$) and considered to be the C_{14} epimeride of *iso*ergosterol.



(VIII.)



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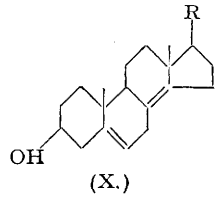

(X.)

All the nuclear double bond positions in the diethenoid sterols were deduced by a method of alleged double bond rearrangement (steroid in ethyl acetate treated with platinum in a nitrogen atmosphere) which Stavely and Bollenback (*J. Amer. Chem. Soc.*, **1943**, **65**, 1600) have subsequently suggested to be most unreliable.

It is not surprising, therefore, that the optical rotatory power data are quite inconsistent with any of the proposed formulations of these yeast fat sterols. It is to be predicted, with a reasonable degree of certainty, that ascosterol and faecosterol both have the nuclear double bond in the same ε-($\Delta^{9:11}$)-position. This is in agreement with the M.R.D.'s of these compounds and, also, the absolute magnitude of their rotatory powers. The alleged rearrangement of ascosterol benzoate to faecosterol benzoate by platinum in ethyl acetate has already been criticised adversely by Stavely and Bollenback (*loc. cit.*) and the anomalous occurrence of such a change has subsequently been doubted by Wieland himself (Wieland and Benend, *loc. cit.*). The optical rotatory power data for episterol are best interpreted on the grounds that this sterol has a γ-nuclear double bond, this agreeing with the observed M.R.D.'s (which are not very reliable) and the absolute magnitude of the molecular rotation (which is more trustworthy). It is not at all likely that the suggested α-ethenoid linkage is actually present. It is not possible, with the limited data available, to make any reliable statement about the structures of anasterol and hyposterol, which also occur as minor constituents of yeast fat.

TABLE V.

Substance.	Formula.	$[M]_D$. *Sterol.*	*Acetate.*	*Benzoate.*	Δ_1.	Δ_2.	References.
7-Dehydrocholesterol	(IX; R = C_8H_{17})	−453	—	−259	—	+194	90, 91.
7-Dehydrocampesterol	(IX; R = C_9H_{17})	−434	—	−251	—	+183	92.
Ergosterol	(IX; R = C_9H_{17})	−515	−372	−345	+143	+170	7, 67, 68, 82, 86, 93, 94, 95, 96.
22 : 23-Dihydroergosterol	(IX; R = C_9H_{19})	−434	−330	—	+104	—	70.
7-Dehydrostigmasterol	(IX; R = $C_{10}H_{19}$)	−426	—	−252	—	+174	90.
7-Dehydroclionasterol	(IX; R = $C_{10}H_{21}$)	−404	−327	—	+ 77	—	97.
7-Dehydrositosterol	(IX; R = $C_{10}H_{21}$)	−478	−322	−279	+156	+199	98.

Optical rotatory power data on doubly unsaturated sterols of the ergosterol type (IX) are correlated in Table V. For this class of steroid Δ_1 is about +120 and Δ_2 about +185. These values are in good agreement with those recorded for neosterol, but not at all similar to the corresponding figures for *iso*dehydrocholesterol (VIII; R = C_8H_{17} and see Table IV). It is suggested, therefore, that the conjugated double bond system of ergosterol is also present in neosterol. This view is supported by the absorption spectra data for neosterol (Wieland and Gough, *loc. cit.*), as the values of $\lambda_{max.}$ recorded for this substance are almost identical with those for ergosterol, whilst the values of $\varepsilon_{max.}$ are very slightly lower for neosterol than for ergosterol. The absorption spectrum of neosterol is not comparable, moreover, with that of *iso*dehydrocholesterol (Windaus, Linsert, and Eckhardt, *Annalen*, 1938, **534**, 22), which has a characteristically low value of $\varepsilon_{max.}$ of about half that observed with 7-dehydrocholesterol and ergosterol.

The presence of the ergosterol chromophore has already been proved by Wieland, Rath, and Hesse (*loc. cit.*), by the isolation of α-dihydroergosterol from the catalytic hydrogenation product of neosterol under conditions for which a double bond shift was unlikely. Since α-dihydroergosterol has now been shown to possess a γ-double bond (see above), it follows that this must also have been present in the original neosterol. As Wieland, Rath, and Hesse (*loc. cit.*) definitely reject the statement of Callow (*Biochem. J.*, 1931, **25**, 87) that neosterol is only a mixed crystal of ergosterol with a smaller proportion of α-dihydroergosterol, it is very difficult to assign a formula to neosterol. Indeed, the evidence examined here is reasonably good proof that neosterol is substantially ergosterol, in spite of the German authors' opinions to the contrary.

A few years ago the α-sitosterol of Anderson (see Heilbron and Jones, *Ann. Rev. Biochem.*, 1940, IX, 135) was shown to be heterogeneous and, in reality, to consist of at least three sterols, α_1-, α_2-, and α_3-sitosterols (Wallis and Fernholz, *J. Amer. Chem. Soc.*, 1936, **58**, 2446; Bernstein and Wallis, *J. Amer. Chem. Soc.*, 1939, **61**, 1903; Gloyer and Schuette, *J. Amer. Chem. Soc.*, 1939, **61**, 1901). The structure of α_1-sitosterol (as X; R = $C_{10}H_{21}$) was proposed by Bernstein and Wallis (*J. Amer. Chem. Soc.*, 1939, **61**, 2308). That this formulation must be incorrect was subsequently pointed out by Bernstein, Wilson, and Wallis (*loc. cit.*) on the basis of optical rotatory data. This latter finding is confirmed by the data on the α-sitosterols presented in Table VI. For comparison satisterol (Kimm, *Sci. Papers Inst. Phys. Chem. Res. Toyko*, 1937, **34**, 637), isolated from the more soluble (α-sitosterol) fractions of the unsaponifiable matter of rice germ oil, δ-sitosterol, calosterol, and the triterpenoid-like sterols agnosterol, lanosterol, cryptosterol, and the tritisterols have been included. It is very likely that δ-sitosterol is a mixture of α-sitosterols incompletely freed from β- and γ-sitosterols. Calosterol, too, must be a mixture of the taraxasterol type (compare Simpson, *J.*, 1944, 283; Hesse, Eilbracht, and Reichender, *Annalen*, 1941, **546**, 233), especially as calotropis resin, from which calosterol is obtained, is known to be a source of taraxasterols as well. Satisterol would seem to be a somewhat impure form of one of the α-sitosterols and, since both wheat germ and rye germ oils contain α-sitosterols, the occurrence of such bodies in rice germ oil is to be anticipated.

TABLE VI.

Substances.	Suggested formula in literature.	[M]D. Sterol.	Acetate.	Benzoate.	Dinitrobenzoate.	Δ_1.	Δ_2.	Δ_3.	References.
α_1-Sitosterol	(X; R = $C_{10}H_{21}$)	− 8	+132	+217	+224	+140	+225	+232	59, 99, 100.
α_1-Dihydrositosterol	(III; R = $C_{10}H_{21}$)	+ 46	+160	—	—	+114	—	—	101.
α_1-*iso*-Dihydrositosterol	(IV; R = $C_{10}H_{21}$)	+128	+192	—	—	+ 64	—	—	101.
α_1-Sitostanol	(I; R = $C_{10}H_{21}$)	+112	+179	—	—	+ 67	—	—	101.
α_2-Sitosterol	$C_{30}H_{49}(OH)$	+ 17	+ 80	+143	+161	+ 63	+126	+144	99, 100.
α_3-Sitosterol	$C_{29}H_{47}(OH)$	+ 16	+ 27	+ 72	+ 85	+ 11	+ 56	+ 69	59, 100.
δ-Sitosterol	$C_{29}H_{47}(OH)$	− 99	−109	− 83	—	− 10	+ 16	—	60.
Calosterol *	$C_{28}H_{43}(OH)$	+400	+460	+610	—	+ 60	+210	—	102.
Satisterol	$C_{27}H_{45}(OH)$	− 58	− 43	+ 74	—	+ 15	+132	—	103.
α-Tritisterol	$C_{30}H_{49}(OH)$	+230 †	+328	—	—	+ 98	—	—	104, 105.
β-Tritisterol	$C_{30}H_{49}(OH)$	+209 †	+262	—	—	+ 53	—	—	104, 105.
Agnosterol	$C_{30}H_{47}(OH)$	+301	+424	+549	—	+123	+248	—	106.
Cryptosterol	$C_{30}H_{49}(OH)$	+251	+300	+376	—	+ 49	+125	—	106.
Lanosterol	$C_{30}H_{49}(OH)$	+247	+262	+392	—	+ 15	+145	—	106.

* Rotations for this substance are for the wavelength, λ = 5461. † These values in alcohol.

TABLE VII.

Steroid type.	Formula.	Δ_1.	Δ_2.	Δ_3.	Remarks.
Stanol	(I)	−34	+ 2	+ 73	Reliable values.
Δ^5-Stenol	(II)	−35	+ 81	+480	Reliable values.
$\Delta^{8:14}$-Stenol	(III)	−40	− 42	+100	Δ_1 and Δ_2 reliable values.
$\Delta^{14:15}$-Stenol	(IV)	−35	+ 30	+ 75	Δ_1 and Δ_2 reliable values.
$\Delta^{7:8}$-Stenol	(V)	− 6	+ 30	+ 90	Δ_1 and Δ_2 fairly reliable.
$\Delta^{8:9}$-Stenol	(VI)	+15	—	—	Not a well studied type.
$\Delta^{9:11}$-Stenol	(VII)	−52	+ 3	+ 90	Fairly reliable values.
α- and β-Amyrin group	—	+ 6	+145	+ 60	Included for the purpose of comparison.
Lupeol group	—	+70	+200	+140	Included for the purpose of comparison.

All the well-characterised substances in Table VI have positive values for Δ_1, whilst the non-conjugated sterols possess negative values for Δ_1 (with the exception of δ-cholestenol). This enables a clear differentiation to be made between naturally occurring sterols of the 3(β)-configuration and substances belonging to the triterpenoid group (see Table VII). It is interesting to speculate, in this connection, that the α-sitosterols may be assigned a C_{30} formulation on re-examination, thus bringing them into the triterpenoid class.

In Table VII are collected the average values for the M.R.D.'s of the various steroid types that have been discussed above. For comparison the values for the two well-characterised triterpenoid groups have been included. The applicability of this table of constants to problems in the sterol field will be appreciated from the examples of its usage detailed above.

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