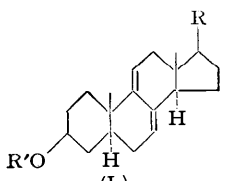
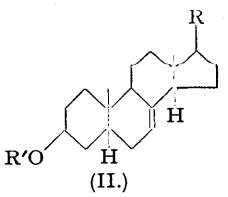
52. *The Application of the Method of Molecular Rotation Differences to Steroids. Part VIII. 22(23)-Dihydroergosterol D.*

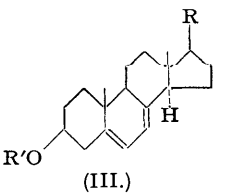
By D. H. R. Barton and J. D. Cox.

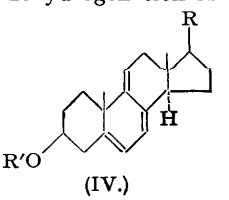
On dehydrogenation with mercuric acetate, γ-ergostenyl acetate furnishes *ergosta*-7(8) : 9(11)-*dien*-3(β)-*yl acetate*. The molecular rotation differences of the latter are identical with those for the corresponding derivatives of ergosterol D and confirm its identity as 22(23)-dihydroergosterol D. The hydrogenation of dehydroergosteryl acetate in neutral solution is briefly reported and discussed.

In Part II of this series (*J.*, 1946, 512) the formula (I; R = C_9H_{17}, R′ = H) was suggested for ergosterol D which, it will be recalled, is prepared by the mercuric acetate dehydrogenation of α-dihydroergosterol (II; R = C_9H_{17}, R′ = H). A similar dehydrogenation of ergosterol (III; R = C_9H_{17}, R′ = H) affords the well characterised dehydroergosterol (IV; R = C_9H_{17}, R′ = H). By analogy it would be expected that the mercuric acetate dehydrogenation of


(I.)


(II.)


(III.)


(IV.)

γ-ergostenol (II; R = C_9H_{19}, R′ = H) would furnish *ergosta*-7(8) : 9(11)-*dien*-3(β)-*ol* (I; R = C_9H_{19}, R′ = H), and this expectation has now been confirmed. In support of the formulated identical position for the conjugated diene system in both ergosterol D and ergosta-7(8) : 9(11)-dien-3(β)-ol we cite the data in Table I, which show that both these alcohols exhibit the same Δ values on acylation. Furthermore the acetates of these two alcohols show identical absorption spectra in the ultra-violet (see Table II). It is fully justified therefore to describe ergosta-7(8) : 9(11)-dien-3(β)-ol as 22(23)-dihydroergosterol D.

Table I.

	$[M]_D$,*					
Substance.	Alcohol.	Acetate.	Benzoate.	Δ_1.	Δ_2.	Refs.
Ergosta-7(8) : 9(11)-dien-3(β)-ol ...	+123°	+128°	+165°	+5°	+42°	Exptl.
Ergosterol D	+ 71	+ 79	+105	+8	+34	Exptl.

* In chloroform.

Table II.

	$\lambda_{max.}$ in mμ.*		$\epsilon_{max.}$	
Substance.	1.	2.	1.	2.
Ergosta-7(8) : 9(11)-dien-3(β)-yl acetate	235	242	13,400	13,400
Ergosteryl D acetate	236	242	11,700	13,200

* In alcohol.

As further evidence in favour of the formula (I; R = C_9H_{17}, R′ = H) for ergosterol D we had planned to make a systematic study of the catalytic hydrogenation of dehydroergosteryl acetate in neutral solution when, from analogy with the behaviour of ergosteryl acetate, it would be expected that selective hydrogenation at the 5(6)-position would occur leading to the formation of ergosteryl D acetate. In the conclusions to be drawn from such experiments we were anticipated by Bergmann and Klacsmann (*J. Org. Chem.*, 1948, **13**, 21), who have studied the hydrogenation of dehydroergosterol with sodium and alcohol and demonstrated that the reduction product, originally called " ergosterol F " (Windaus *et al.*, *Annalen*, 1930, **477**, 268), is actually a mixture of ergosterol, ergosterol D, and α-dihydroergosterol. Such a mixture must be formed by initial 1 : 2-addition of hydrogen to either end of the conjugated trienoid system. The hydrogenation of dehydroergosterol in neutral solution using a platinum catalyst, until slightly over one molecular proportion of hydrogen had been absorbed, furnished a mixture which, by its absorption spectrum, contained 42% of ergosterol D and 8% of unchanged dehydroergosterol. The rotation corresponded closely to that required by such a mixture with α-dihydroergosterol as the constituent transparent in the ultra-violet. The presence of α-dihydroergosterol was confirmed by conversion of the alcohol mixture into the acetate and recrystallisation whereby α-dihydroergosteryl acetate was readily isolated. Since our results in the catalytic hydrogenation experiments were in such close agreement with the conclusions of Bergmann and Klacsmann (*loc. cit.*) it has not been considered desirable to extend the experiments.

Experimental.

(M. p.s are uncorrected.)

The substances whose rotations are listed below were dried in a vacuum, before weighing, at 20° below their m. p.s, or at 120°, whichever was the lower temperature. All rotations are for the Na_D line and in chloroform solution. They were taken in 1 dm. macro- or micro-tubes, the use of the latter being specifically indicated after each recorded measurement.

Standard chemical operations were carried out as in Part IV (*J.*, 1948, 783), unless specified to the contrary.

Micro-analyses are by Drs. Weiler and Strauss, Oxford.

Ergosta-7(8) : 9(11)-*dien*-3(β)-*ol and Derivatives.*—720 Mg. of ergost-7(8)-en-3(β)-yl acetate (Part IV, *loc. cit.*) were dissolved in 25 ml. of alcohol. 1·50 G. of mercuric acetate (145% theory) dissolved in 25 ml. of alcohol acidified with a few drops of acetic acid were added and the mixture refluxed for one hour on the water-bath. The solvent was removed under reduced pressure, the residue extracted with benzene, and the extract filtered through alumina. From the filtrate there was obtained *ergosta*-7(8) : 9(11)-*dien*-3(β)-*yl acetate*, m. p. 151—152° after crystallisation from chloroform–methanol, $[\alpha]_D$ +29° (*c*, 1·69; micro-tube) $[M]_D$ +128° (Found : C, 80·7, 81·3; H, 10·9, 10·4. $C_{30}H_{48}O_2$ requires C, 81·8; H, 10·9%). For the absorption spectrum see Table II. Alkaline hydrolysis of this acetate afforded *ergosta*-7(8) : 9(11)-*dien*-3(β)-*ol*, recrystallised from ethyl acetate–methanol; m. p. 139·5—140·5°, $[\alpha]_D$ +31° (*c*, 1·14; micro-tube), $[M]_D$ +123° (Found : C, 81·0, 80·8; H, 12·2, 11·6. $C_{28}H_{46}O$ requires C, 84·4; H, 11·6. $C_{28}H_{46}O,H_2O$ requires C, 80·8; H, 11·5%). Benzoylation furnished *ergosta*-7(8) : 9(11)-*dien*-3(β)-*yl benzoate*, recrystallised from chloroform–methanol; m. p. 151—152°, $[\alpha]_D$ +33° (*c*, 1·12; micro-tube), $[M]_D$ +165° (Found : C, 82·7; H, 10·0. $C_{35}H_{50}O_2$ requires C, 83·6; H, 10·0%).

Hydrogenation of Ergosta-7(8) : 9(11)-*dien*-3(β)-*yl Acetate.*—20 Mg. of ergosta-7(8) : 9(11)-dien-3(β)-yl acetate were dissolved in 20 ml. of 1 : 1 ether–acetic acid and shaken with 100 mg. of platinum catalyst in an atmosphere of hydrogen for 6 hours. 15 Mg. of α-ergostenyl acetate, m. p. 108—109°, mixed m. p. with an authentic specimen (m. p. 108—109°) also 108—109°, were obtained.

Ergosterol D and Derivatives.—1·40 G. of pure α-dihydroergosteryl acetate (Part V) were treated in acetic acid-acidified alcoholic solution with 2·5 g. of mercuric acetate as described above. After working up as for ergosta-7(8) : 9(11)-dien-3(β)-yl acetate and recrystallisation from ethyl acetate–methanol, ergosteryl D acetate, m. p. 169°, $[\alpha]_D$ +18° (*c*, 2·03; micro-tube), $[M]_D$ +79°, was isolated. Alkaline hydrolysis afforded ergosterol D, recrystallised from ethyl acetate–methanol; m. p. 163°, $[\alpha]_D$ +18° (*c*, 1·38; micro-tube), $[M]_D$ +71°. Benzoylation of ergosterol D gave *ergosteryl D benzoate*, recrystallised from ethyl acetate; m. p. 174—176°, $[\alpha]_D$ +21° (*c*, 2·43; micro-tube), $[M]_D$ +105° (Found : C, 83·3; H, 9·8. $C_{35}H_{48}O_2$ requires C, 84·0; H, 9·6%).

Dehydroergosterol.—This substance, prepared from ergosterol by the method of Windaus and Linsert (*Annalen*, 1928, **465**, 148), was recrystallised from ethyl acetate–methanol; m. p. 142—144°, $[\alpha]_D$ +150° (*c*, 1·80). Acetylation afforded dehydroergosteryl acetate, purified by chromatography and recrystallisation from chloroform–methanol; m. p. 145—146°, $[\alpha]_D$ +195° (*c*, 2·85).

Hydrogenation of Dehydroergosterol in Neutral Solution.—960 Mg. of dehydroergosterol, dissolved in 60 ml. of ethyl acetate, were shaken with 100 mg. of reduced platinum catalyst in an atmosphere of hydrogen until 72 ml. of hydrogen had been absorbed (theory for 1 double bond was 60 ml.). After removal of the catalyst by filtration and the solvent under reduced pressure, two recrystallisations of the residue from ethyl acetate–methanol gave a substance, m. p. 159—161°, $[\alpha]_D$ +12° (*c*, 2·10). These constants approximate to those recorded above for ergosterol D, but the absorption spectrum (in alcohol) showed that 42% of ergosterol D and 8% of unchanged dehydroergosterol were present. Ergosterol (cf. Bergmann and Klacsmann, *J. Org. Chem.*, 1948, **13**, 21) was not present. The other component in the mixture was doubtless α-dihydroergosterol, since $[\alpha]_D$ calculated for such a mixture would be +10°, in agreement with the observed value. This suggestion was confirmed by conversion of the mixture into

the acetates and repeated recrystallisation from ethyl acetate–methanol, when α-dihydroergosteryl acetate, m. p. 180°, was isolated.

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