rose rapidly from −20° to 0°, and there was formed a mass of white solid. The reaction mixture was quickly cooled again to −20°, and the rest of the base was added slowly. The mixture turned a red-violet color after 20 min., and at the end of 30 min. the reaction was stopped by the addition of hydrochloric acid. Upon extraction with chloroform, a brown oil which was not identified separated from the aqueous phase, producing three phases. The chloroform extract was worked up in the usual manner, yielding 19.1 g. (20.7%) of a light yellow liquid, b.p. 86–87° (0.07 mm.), which crystallized on standing. This product was recrystallized from ether at −20°, m.p. 40°, with an infrared spectrum identical with that reported above.

Ultraviolet spectra.—The ultraviolet spectra of the pyridalacetones were run in water and ethanol at concentrations from 1.0×10^{-5} to 7.0×10^{-5} molar (Table I).

URBANA, ILL.

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Influence of a 9(11)-Double Bond on the Course and Mechanism of Alkyl-Oxygen Cleavage Reactions of Unsaturated Steroids*

WILLIAM R. NES AND JOHN A. STEELE

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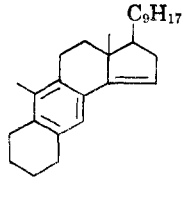
The rate of the buffered solvolysis of dehydroergosteryl tosylate was found to be slightly slower than the solvolysis rate of ergosteryl tosylate which indicates no homoallylic participation of the 9(11)-double bond in this reaction. The product of solvolysis of ergosteryl tosylate was 3,5-cyclo-7,22-ergostadien-6β-ol (XV) and not the isomeric 3,5-cyclo-6,22-ergostadien-8-ol when prepared in boiling aqueous acetone containing potassium bicarbonate. The same conditions yielded *i*-dehydroergosterol from dehydroergosteryl tosylate and the kinetic data together with the conditions of its preparation prove that the original formulation of this compound as 3,5-cyclo-7,9(11),22-ergostatrien-6β-ol (III) is correct. The failure of the 9(11)-double bond to participate in a typical homoallylic reaction makes it difficult or impossible to account for the acid-catalyzed elimination reaction of dehydroergosterol on the basis of a homoallylic mechanism. In the acid-catalyzed conversion of dehydroergosterol to 5,7,9(11),14,22-ergostapentaene (VI) the hypothesis is offered that the 5-double bond migrates first into the 4-position (I → IV) and that the dehydration proceeds by an allylic mechanism (IV → V).

The acid-catalyzed reactions of 3,5-cyclo-7,22-ergostadien-6β-ol (*i*-ergosterol, XV) and of 3,5-cyclo-7,9(11),22-ergostatrien-6β-ol (*i*-dehydroergosterol, III) in ethanol were also studied quantitatively and qualitatively. The 9(11)-dehydro compound (III) reacted *ca.* 50% faster than XV. This is considered as evidence that the 9(11)-double bond participates in allylic alkyl-oxygen cleavage to but a small extent. *i*-Ergosterol yielded *ca.* 70% of an *i*-hydrocarbon (3,5-cyclo-6,8(14),22-ergostatriene, XVI) and *ca.* 30% of ergosteryl ethyl ether while *i*-dehydroergosterol yielded *ca.* 85% of dehydroergosteryl ethyl ether (X) and *ca.* 15% of an *i*-hydrocarbon [3,5-cyclo-6,8(14),9(11),22-ergostatetraene (VIII)]. The influence of the 9(11)-double bond on the course of this acid-catalyzed reaction is interpreted, *inter alia*, as a conformational effect. Ergosteryl tosylate when submitted to hot pyridine readily underwent elimination to give the *i*-hydrocarbon, but dehydroergosteryl tosylate failed to react analogously and a conformational influence of the 9(11)-double bond is also suggested for this reaction.

Preparative conditions for obtaining 3,5-cyclo-6,8(14),22-ergostatriene and 3,5-cyclo-6,8(14),9(11),22-ergostatetraene are described.

When dehydroergosterol (I) and its derivatives undergo alkyl-oxygen cleavage at C-3, two types of initial product have been shown to arise depending on the conditions of the reaction and the nature of the esterifying group. Thus, solvolysis of the tosylate (II) in aqueous acetone leads to rearrangement and the production of a 3,5-cyclosterol (*i*-dehydroergosterol) for which structure III (3,5-cyclo-7,9(11),22-ergostatrien-6β-ol) has been suggested,[1] while treatment of the free alcohol (I) with hydrogen chloride in chloroform leads to dehydration and the formation of unrearranged hydrocarbons such as 5,7,9(11),14,22-ergostapentaene (VI),[2] which can further undergo a rearrangement to give anthraergostapentaene (VII).[3a,3b] That the anthrasteroid rearrangement[3] proceeds as

(3b) Note added in proof: A. W. Burgstahler (Abstracts of papers presented before the New York meeting of the American Chemical Society, September 8–13, 1957, page 25P) has recently achieved hydroxylation of an analog, anthracholestatetraene (W. R. Nes, R. B. Kostic and E. Mosettig, *J. Am. Chem. Soc.*, **78**, 436 (1956)), of VII with osmium tetroxide. The resulting glycol was cleaved with lead tetraacetate yielding a keto-aldehyde which underwent a reverse Michael reaction to give a tricyclic ketone which in turn on reduction with lithium aluminum hydride followed by dehydrogenation furnished 3,9-dimethylanthracene. It has previously been shown in this laboratory that the anthrasteroid rearrangement involves scission of either the C_1–C_{10} bond or the C_9–C_{11} bond.[3] Burgstahler's work establishes that the former is correct. Were the latter true, he would have obtained 2,9-dimethylanthracene. It follows from his degradation that the complete structure of VII is



* This paper is a contribution in honor of Lyndon F. Small, former Editor of the Journal.

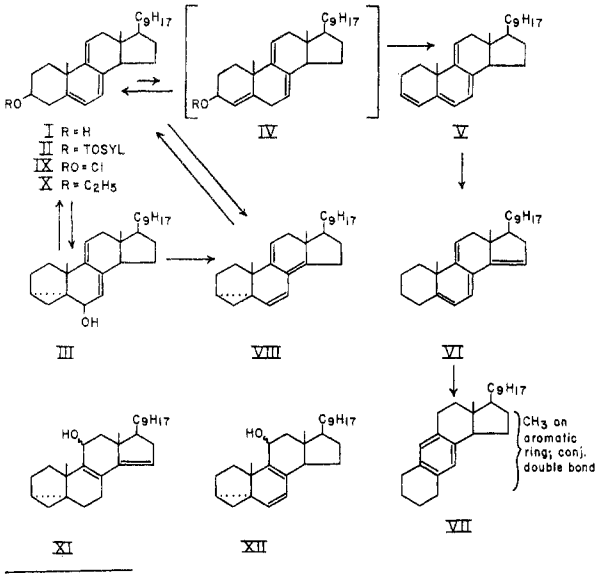
(1) R. W. Rees and C. W. Shoppee, *J. Chem. Soc.*, 3422 (1954).

(2) W. R. Nes, *J. Am. Chem. Soc.*, **78**, 193 (1956).

(3a) W. R. Nes and E. Mosettig, *J. Am. Chem. Soc.*, **75**, 2787 (1953); **76**, 3182 (1954).

a subsequent process to the dehydration has been demonstrated experimentally.[2] The present work was undertaken (*a*) to elucidate the mechanism of this acid-catalyzed dehydration and (*b*) to eliminate or confirm an alternate structure[4] [3,5-cyclo-8,14,-22-ergostatrien-11-ol, (XI)] for *i*-dehydroergosterol.

The ease with which these two types of alkyl-oxygen cleavage reaction occur at C-3 suggests that they may be taking place by the same mechanism. Much work,[5,6] has shown that homoallylic participation (1,3-interaction between the π-electrons of a double bond and a reaction center) is responsible for many of the facilitated reactions of sterols unsaturated in ring B, and it is clear that the solvolysis of the tosylate (II) proceeds by this mechanism, because a 3,5-cyclosteroid is produced. It remains only to decide between the alternate structures (III or XI).[4] The ultraviolet spectrum[1,2,4] (λ_{max} 247, ϵ 16,400) of the isolated product leaves only these two possibilities. One of them (III) would arise by the major involvement of the 5-double bond in the reaction; the other (XI) would be a product of bond migration of 3,5-cyclo-6,8,22-ergostatrien-11-ol (XII) which would arise by the complete participation of all three of the double bonds in the reaction. Much less evident is the degree to which homoallylic participation contributes to the mechanism of the acid-catalyzed elimination. A possibility that it might be involved was found in the variation of the rate of disappearance of the 5,7,9(11)-triene system with changes in the substituent at C-3 (20-fold difference between the hydroxy and 3,5-dinitrobenzoxy compounds).[2] On the other hand, a likely intermediate, 3,5-cyclo-6,8(14),9(11),22-ergostatetraene (VIII), has been excluded, because under the conditions of the elimination reaction with less than stoichiometric amounts of HCl as the catalyst the hydrocarbon (VIII) consumed the HCl by addition yielding dehydroergosteryl chloride (IX) in the equivalent amount.[2]



Dehydroergosterol in the presence of less than stoichiometric amounts of HCl underwent elimination.[2] Another possible intermediate from homoallylic participation is *i*-dehydroergosterol (III), but it has been shown that this likewise undergoes the retro-*i*-steroid rearrangement in acid solution.[4] The reaction was carried out in aqueous acetone and the product was dehydroergosterol (I). We have now extended this to ethanol and have obtained dehydroergosteryl ethyl ether (X) in a high yield. The failure of either III or VIII to be demonstrable intermediates in the acid-catalyzed conversion of I to VI makes it very unlikely that homoallylic participation does in fact contribute significantly to this reaction *unless* this participation occurs without the real formation of a 3,5-cyclosteroid. Shoppee, Summers, and Williams[7] have obtained evidence to show that 1,3-interaction is involved in the reactions of 7-hydroxy-Δ^4-steroids although a cyclopropyl ring does not actually close. It was felt that the question could be settled in the present case by comparing the rate of solvolysis of ergosteryl tosylate (XIV) with that of dehydroergosteryl tosylate (II). There is a great difference in the reactions of ergosterol (XIII) and dehydroergosterol (I) under acid conditions; the latter undergoes dehydration while the former does not.[3] If this increase in the ease of alkyl-oxygen cleavage were due to increased homoallylic participation resulting from an extension of the conjugated system, *i.e.* the change from a 5,7-dienol (XIII) to a 5,7,9(11)-trienol (I), then a similar enhancement in the rate of alkyl-oxygen cleavage would be expected in the solvolysis of the 5,7,9(11)-trienyl tosylate (II) compared to the 5,7-dienyl tosylate (XIV). A comparison of these rates would also indicate whether the *i*-dehydroergosterol resulting from the solvolysis of II could possess an 11-hydroxyl group (XI or XII), because participation of all three double bonds should manifest itself not only in the structure of the product but as well in an enhanced rate of reaction. This expectation rests, among other things, on the

The mechanism of the rearrangement, as first suggested by P. Bladon (*J. Chem. Soc.*, 2176 (1955)), probably follows a course analogous to that of the dienone-phenol rearrangement (R. B. Woodward and T. Singh, *J. Am. Chem. Soc.*, **72**, 494 (1950)).

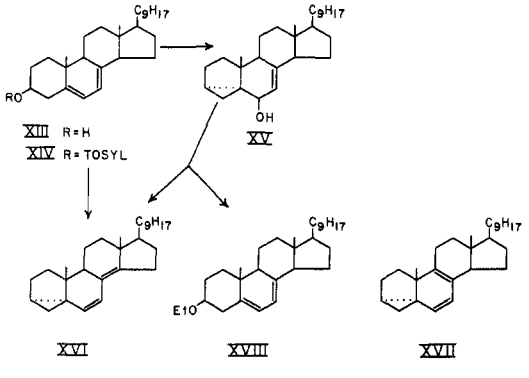
(4) W. R. Nes and C. W. Shoppee, *J. Chem. Soc.*, **93** (1957).

(5) (a) M. Simonetta and S. Winstein, *J. Am. Chem. Soc.*, **76**, 18 (1954); (b) E. M. Kosower and S. Winstein, *J. Am. Chem. Soc.*, **78**, 4347 (1956) and the references cited therein.

(6) (a) C. W. Shoppee and D. F. Williams, *J. Chem. Soc.*, 2488 (1956); (b) C. W. Shoppee and G. H. R. Summers, *J. Chem. Soc.*, 3361 (1952) and the references cited therein.

(7) C. W. Shoppee, G. H. R. Summers, and R. J. W. Williams, *J. Chem. Soc.*, 1893 (1956). Solvolysis of ψ-cholesteryl tosylate gave 4-cholesten-7β-ol, *i.e.* the reaction took place with retention of configuration.

findings[8] that the rate of solvolysis of steroidal tosylates rises sharply with the number of double bonds in ring B, *viz.*, a 100-fold and a 3000-fold increase for the introduction, respectively, of a 5-double bond and a 5,7-diene system into a saturated sterol. Extrapolation of these figures suggests a further 10-fold increase on going from a 5,7-dienyl tosylate (XIV) to a 5,7,9(11)-trienyl tosylate (II). The interpretation of these comparative rates to the problem of the structure of *i*-dehydroergosterol rests on the assumption that the isolated product does not result from a secondary isomerization, *e.g.* III to XII. It was necessary first to insure that this assumption was valid, and so the preparation of *i*-dehydroergosterol was carried out under conditions so buffered (potassium bicarbonate in a boiling solution) that the reaction mixture remained alkaline. The original conditions[1,2,4] using the salt (potassium acetate) of a nonvolatile weak acid yielded a solution with a *p*H below 7 when the liberated *p*-toluenesulfonic acid was neutralized. The modified conditions, which constitute by far the best preparative method, gave the same *i*-dehydroergosterol as had been obtained previously. These findings, of course, anticipate the results of our kinetic measurements, for of the two possible structures (III and XI) for *i*-dehydroergosterol one of them (XI) requires that bond migration has taken place (XII → XI) under what almost certainly would have to be acid conditions.



We have prepared ergosteryl and dehydroergosteryl tosylates (XIV and II) essentially according to the procedures reported in the literature[1,9] but with some improvement in the former case. They were submitted to solvolysis in ethanol at 30° in the presence of potassium acetate. The rates of disappearance of the respective polyene systems were followed spectrophotometrically, and it was found that the half-life was 1.64 hr. for ergosteryl tosylate (XIV) and 2.16 hr. for dehydroergosteryl tosylate (II). This is illustrated graphically in Figure 1 in which the logarithm of the intensity of the ultraviolet absorption of the diene and triene systems

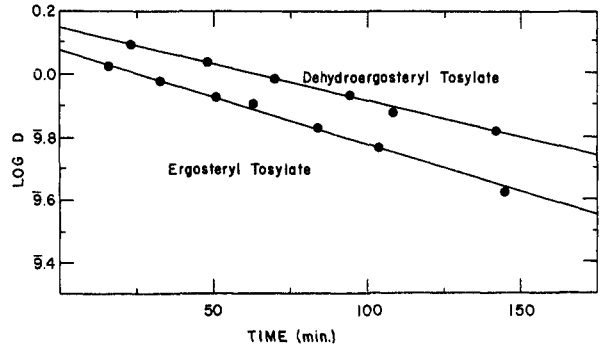


FIG. 1. DISAPPEARANCE OF ERGOSTERYL TOSYLATE (XIV) AND DEHYDROERGOSTERYL TOSYLATE (II) in ethanol buffered with potassium acetate at 30° as observed from the disappearance of absorption at 294 mμ (XIV) and 340 mμ (II). D = optical density.

is plotted as a function of time. It is evident that dehydroergosteryl tosylate actually reacts slightly slower than ergosteryl tosylate rather than several times faster. *One can conclude from this that the 9(11)-double bond does not participate significantly in homoallylic reactions involving C-3.* Furthermore, one can infer (*a*) that homoallylic participation cannot account for the difference in reactivities of ergosterol and dehydroergosterol under acid conditions and, therefore, cannot be involved in the mechanism of the acid-catalyzed elimination (I to VI), and (*b*) that *i*-dehydroergosterol is 3,5-cyclo-7,9(11),22-ergostatrien-6β-ol (III). This structure (III) for *i*-dehydroergosterol was the one originally suggested by Rees and Shoppee[1] and there seems to be no further reason to question it. The assignment of the beta configuration to the 6-hydroxyl group is based on analogy with the configuration of the hydroxyl group in other 3,5-cyclosteroids.[10] The *i*-steroid rearrangement of ergosteryl tosylate (XIV) to an *i*-sterol has not been previously described in the literature, although Fieser, Rosen, and Fieser[11] have shown that the elimination of *p*-toluenesulfonic acid from XIV in the absence of hydroxylic solvents leads to an *i*-hydrocarbon [3,5-cyclo-6,8(14),22-ergostatriene, XVI]. We have submitted ergosteryl tosylate (XIV) to buffered solvolysis in the presence of potassium bicarbonate in aqueous acetone and have isolated in a 90% yield a product which exhibits end-absorption in the ultraviolet with an extinction coefficient at 220 mμ of 2100 and a low intensity maximum (ε 790) at 262 mμ. The latter band corresponds to a 3% content of 3,5-cyclo-6,8(14),22-ergostatriene (XVI). The purified *i*-sterol (λ_{max} 2.76 μ) showed only the end-absorption in the ultraviolet with an extinction coefficient of 1300 at 220 mμ. This absorption is characteristic of Δ^7-steroids and atyp-

(8) See M. Simonetta and S. Winstein[5a] for references and a quotation of unpublished experiments.

(9) P. Karrer and H. Asmis, *Helv. Chim. Acta*, **35**, 1926 (1952).

(10) For a searching analysis of the evidence for the *beta* configuration ref. 5(b) should be consulted together with the paper of D. E. Evans and G. H. R. Summers, *J. Chem. Soc.*, 906 (1957).

(11) M. Fieser, W. E. Rosen, and L. F. Fieser, *J. Am. Chem. Soc.*, **74**, 5397 (1952).

ical of Δ^6-steroids in which the double bond is conjugated with the 3-membered ring. The end-absorption of the former[12] have extinction coefficients of *ca.* 1500 at 220 mμ and the latter[13] have extinction coefficients of *ca.* 8000 at this wave length. This establishes the structure of *i*-ergosterol as 3,5-cyclo-7,22-ergostadien-6β-ol (XV) in which the 6-hydroxyl group is assigned the beta configuration by analogy.[10] The conversion of ergosteryl tosylate predominantly to this compound and not the isomeric 8-hydroxy-Δ^6-derivative is analogous to the reduction of the same starting material to 3,5-cyclo-7,22-ergostadiene with lithium aluminum hydride.[9] It is also analogous to the conversion of dehydroergosteryl tosylate (II) to an *i*-dehydroergosterol with the structure III and the similarity of III and XV is in accord with the kinetic data for the solvolysis reactions. All of these facts are in agreement with the proposition that the major contribution to homoallylic participation is made by the 5-double bond and that the 9(11)-double bond plays little or no electronic role. The contribution which the 7-double bond makes as illustrated by a 30-fold enhancement in the rate of solvolysis of 7-dehydrocholesteryl tosylate compared to cholesteryl tosylate[8] is apparently of the kind which was found[7] for the 7-hydroxy-Δ^4-steroids. The ease with which a 5-double bond can disassociate itself from a 7-double bond is also exemplified in the oxidation of ergosterol (XIII) to ergosterone (4,7,-22-ergostatrien-3-one).[14] The double bond is brought into conjugation with the α,β-unsaturated ketone moiety with HCl in methanol but only as a result of passing through the enol ether (3-methoxy-3,5,7,22-ergostatetraene).[15] The failure of the 9(11)-double bond to give any indication of participating in a homoallylic reaction suggested a study of whether it would produce a marked effect in an allylic reaction. The *i*-sterols (III and XV) presented suitable allylic systems for comparison. They should undergo acid-catalyzed alkyl-oxygen cleavage at rates proportional to the extent of participation of the 9(11)-double bond.[16] We have measured the rates at which *i*-ergosterol (XV) and *i*-dehydroergosterol (III) undergo this reaction in 0.00020*M* ethanolic oxalic acid solution containing 0.4% water. The disappearance of the characteristic maximum at 247 mμ for III could be followed directly (Figure 3). The appearance of the characteristic maximum at 340 mμ for one of the products

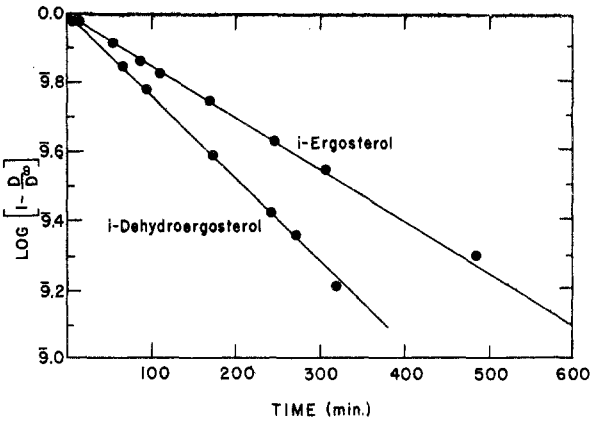


FIG. 2. DISAPPEARANCE OF *i*-ERGOSTEROL (XV) AND *i*-DEHYDROERGOSTEROL (III) in 0.00020*M* ethanolic oxalic acid solution containing 0.4% water at 30° as calculated from the appearance of the absorption at 262 mμ (XVI) for XV and at 340 mμ (X) for III. D = optical density.

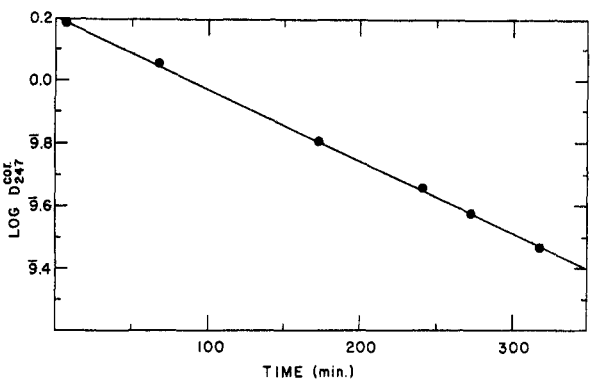


FIG. 3. DISAPPEARANCE OF *i*-DEHYDROERGOSTEROL (III) in 0.00020*M* ethanolic oxalic acid solution containing 0.4% water at 30° as observed from the disappearance of absorption at 247 mμ (III) using a correction for the appearance of absorption at this wave length for VIII and X. D = optical density.

(X) could also be followed (Figure 2) simultaneously and the half-life of *i*-dehydroergosterol (III) as calculated from either measurement was 2.2 hr. The half-life of *i*-ergosterol (XV) could only be calculated from the rate of appearance of the characteristic maxima at 262 and 294 mμ for the products (XVI and XVIII) (Figure 2), because XV has no absorption in the usable region of the ultraviolet which is not greatly interfered with by the absorption of the products. The half-life of *i*-ergosterol was 3.3 hr. It is likely that the corresponding ethyl ethers of III and XV are formed during the course of this reaction. These compounds would have the same absorption as the alcohols and our measurements may actually comprise a comparison of the rates of reaction of the ethers. The increase of less than 100% in the rate of reaction when the 9(11)-double bond was introduced indicates that it does participate in allylic reactions to a small extent. However, its influence is very much smaller than, for instance, the effect of a second double bond (Δ^7) on the solvolysis of cholesteryl tosylate.[8] The presence

(12) P. Bladon, H. B. Henbest, and G. W. Wood, *J. Chem. Soc.*, 2737 (1952).

(13) I. M. Klotz, *J. Am. Chem. Soc.*, **66**, 88 (1944).

(14) R. J. Oppenauer, *Rec. trav. chim.*, **56**, 137 (1937).

(15) D. A. Shepherd, R. A. Donia, J. A. Campbell, B. A. Johnson, R. P. Holysz, G. Slomp, Jr., J. E. Stafford, R. L. Pederson, and A. C. Ott, *J. Am. Chem. Soc.*, **77**, 1212 (1955).

(16) For a discussion of acid-catalyzed alkyl-oxygen cleavage reactions from a kinetic and mechanistic point of view see C. K. Ingold, *Structure and Mechanism in Organic Chemistry*, Cornell University Press, Ithaca, N. Y., 1953, p. 779.

of the 9(11)-double bond manifests itself to a larger extent in a difference in the composition of the products which are obtained from III and XV. *i*-Ergosterol (XV) yielded an approximately 2:1 mixture of 3,5-cyclo-6,8(14),22-ergostatriene (XVI) and ergosteryl ethyl ether (XVIII), but *i*-dehydroergosterol (III) yielded an approximately 1:5 mixture of the corresponding products (VIII and X). There are several possible reasons why introduction of the 9(11)-double bond decreases the extent of elimination relative to retro-*i*-steroid rearrangement. One of these is a greater charge distribution on the intermediate carbonium ion which might decrease the rate at which the proton at C-14 is eliminated, but the kinetic results suggest that this may not be very significant. A factor which may make a larger contribution is that the presence of the 9(11)-double bond reduces by 50% the number of tertiary hydrogen atoms which could be eliminated. *i*-Ergosterol may actually yield, in addition to XVI, 3,5-cyclo-6,8,22-ergostatriene (XVII) which is rapidly isomerized to the more stable isomer (XVI) with a heteroannular diene system. Another possibility is that the conformation of the molecule is changed such that the stereochemical requirements of elimination are satisfied less well in the presence of the 9(11)-double bond than they are in its absence. There is another reason for implicating a conformational influence of the 9(11)-double bond in the reactions of unsaturated steroids. We have submitted ergosteryl and dehydroergosteryl tosylates to treatment with pyridine at 100° and find that ergosteryl tosylate (XIV) is converted to the *i*-hydrocarbon (XVI) in a good yield in *ca.* 17 min. Contrariwise, dehydroergosteryl tosylate undergoes elimination to the extent of only a few percent (yielding VIII) even after 4 hr. Since this elimination reaction to the respective *i*-hydrocarbons is a homoallylic reaction and since the two tosylates solvolyze in ethanol at approximately the same rate, this result is not readily explained on the basis of an electronic influence of the 9(11)-double bond, and a conformational explanation seems more plausible. The small yield of *i*-hydrocarbon from the treatment of dehydroergosteryl tosylate with pyridine is in accord with the small proportion of *i*-hydrocarbon obtained from the acid-catalyzed reaction of *i*-dehydroergosterol and the high yield of *i*-hydrocarbon from ergosteryl tosylate agrees with the high yield from *i*-ergosterol.

The treatment of ergosteryl tosylate with hot pyridine was an easy method for the preparation of 3,5-cyclo-6,8(14),22-ergostatriene (XVI).[17] A slightly purer product, however, was obtained by proceeding through XV. A good method for the preparation of the 9(11)-dehydro analog (VIII)[17] was found in the treatment of *i*-dehydroergosterol (III) with trichloroacetyl chloride in excess pyridine at room temperature. Under these conditions the trichloroacetate underwent elimination. When the reaction was carried out in a benzene solution in the presence of only a slight excess of pyridine and the solution was washed with a cold bicarbonate solution, the product was composed of a large amount of dehydroergosterol resulting from solvolysis of the trichloroacetate with retro-*i*-steroid rearrangement. The benzoate and the *p*-nitrobenzoate[1] of *i*-dehydroergosterol, though not isolated crystalline, were apparently stable, for on alkaline hydrolysis *i*-dehydroergosterol was recovered. 3,5-Dinitrobenzoylation gave the *i*-hydrocarbon (VIII).

Since homoallylic participation does not account for the mechanism of the acid-catalyzed elimination reaction of dehydroergosterol (I), the question is unanswered as to why dehydration should take place more readily with I than with ergosterol (XIII) or, for that matter, why it should take place readily at all. The suggestion is offered, therefore, that the dehydration is an allylic rather than a homoallylic reaction and that it is preceded by migration of the 5-double bond [and less likely the 7- and/or 9(11)-double bonds] into conjugation with the C-O linkage at C-3. A rapid equilibration of dehydroergosterol (I) with a compound such as 4,7,9(11),22-ergostatetraen-3β-ol (IV, R = H) in which the latter existed only in a relatively small amount would account for the observed facts, namely, that facile dehydration takes place and that there is a relationship between the substituent at C-3 and the disappearance of the triene system.[2] The apparent 1,3-interaction would thus be a kinetic consequence of having a two-step process in which the first (I → IV) is rapid equilibration and the second (IV → V) a slow, irreversible and rate-determining step. This sequence of reactions

(17) The presence of smaller amounts of other hydrocarbons in various preparations of VIII and XVI have been considered in previous publications.[4,11] It was found that a hydrocarbon with a maximum at 252 mμ was formed in addition to VIII in the retro-*i*-steroid rearrangement of III.[1,2,4] In the present investigation the sample of VIII which was isolated from the retro-*i*-steroid rearrangement of III in ethanol buffered with potassium bicarbonate displayed a spectrum with an exaggerated intensity of absorption near 244 mμ relative to that at 295 mμ (the second band of VIII) in qualitative though not quantitative agreement with previous work. No explanation for the origin or structure of this material is yet at hand. The hydrocarbon (VIII) was readily obtained pure by the elimination of trichloroacetic acid from the trichloroacetate of III in pyridine. The elimination of *p*-toluenesulfonic acid from II gave only an impure preparation of VIII in 3% yield, but the contaminant was not the same as in the retro-*i*-steroid rearrangement. The hydrocarbon(s) which accompany XVI when it is prepared by dehydration of ergosterol with *p*-toluenesulfonyl chloride has been studied by rotational measurements[11] but no structure was arrived at. We have found that XVI when prepared by the elimination of p-toluenesulfonic acid from pure XIV is accompanied by a hydrocarbon with absorption near 290 mμ. It is possible, although by no means certain, that the contaminant is XVII. The sample of XVI which is obtained by elimination of water from *i*-ergosterol (XV) is obtained readily in at least 97% purity.

would require that an intermediate be 3,5,7,9(11),-22-ergostapentaene (V). We have not as yet isolated this compound, but in the course of the many reactions which have been carried out in connection with the anthrasteroid rearrangement in this laboratory we have often observed the characteristic spectrum (λ_{max} *ca.* 335, 353, and 370 mμ) of this compound (V) in chromatographic eluates. The amount has always been small. Even more significant is that as these reactions were followed spectrophotometrically these long wave-length bands could be discerned early in the reaction. An alternate to an allylic mechanism is one which proceeds directly from dehydroergosterol by production of a carbonium ion with a charge distribution centered around C-3 and the transfer of a hydride ion from C-4 to C-3 followed by elimination of a proton at C-14 and/or C-12. The detection of V in the reaction mixture, however, supports the allylic hypothesis. Furthermore, the mechanism involving a hydride ion shift is really a modification of homoallylic participation which has been rendered untenable. The only difficulty with the allylic mechanism is that the bond migration reaction has not been observed experimentally with 5,7,9(11)-trienols. Nevertheless, there is a precedent for it in the stability of 3,3-(ethane-1,2-dithiyl)-4,7,22-ergostatriene (ethylene thioketal of ergosterone) as opposed to the isomer with a 5,7-diene system. The former is obtained under conditions (zinc chloride) which could cause isomerization.[18] On the other hand, the bond is stable in the 5-position in the corresponding 3,3-dioxy derivative (ethylene ketal of ergosterone).[18] This sensitivity to slight changes in the molecule indicates a small energy difference between the 4- and 5-positions in keeping with the proposal that the $\Delta^{4,7,9(11),22}$-steroid (IV) might exist in equilibrium with dehydroergosterol (I). It is also in accord with the ease with which the 5-double bond can disassociate itself from a 7-double bond as discussed above in connection with the oxidation of ergosterol. The differential in reactivity between ergosterol and dehydroergosterol would then be a consequence of a differential in the rate of the bond migration reaction with the two compounds (I and XIII) and/or in the stability of the isomerized products. The influence of the 9(11)-double bond on this reaction could be a conformational one.

EXPERIMENTAL[19]

Preparation of ergosteryl and dehydroergosteryl tosylates. The sterol (10 g.) was dried by dissolving it in benzene and removing the solvent under reduced pressure. It was then dissolved in pyridine (125 ml. for XIII and 50 ml. for I) and 12 g. of *p*-toluenesulfonyl chloride (freshly recrystallized three times from petroleum ether, b.p. 60–70°) was added. The reaction mixture was allowed to remain at room temperature in the dark overnight and was then poured into a liter of ice cold 4% aqueous potassium bicarbonate solution. The resulting solid tosylate was collected by filtration, washed well with water (and, in the case of II, with a little cold ethanol), and dried in a high vacuum at 37°. The ergosteryl tosylate (XIV) so obtained weighed 13.6 g. but contained some *i*-hydrocarbon (XVI) as shown by ultraviolet assay. It was very sensitive as noted in the literature[9,11] and reproducible results could not be obtained by the reported procedure for its purification.[9] A good product could be obtained consistently, however, by stirring the tosylate (13.6 g.) in 50 ml. of ether at 0° for 1 hr. followed by refrigeration at −20° overnight. This procedure removed the *i*-hydrocarbon without extensive decomposition of the tosylate. The product weighed 8.0 g. and could then be recrystallized from acetone by dissolving it rapidly in a small amount of the hot solvent and immediately cooling to 0° or below. Two such recrystallizations yielded XIV as a colorless mixture of needles and prisms, m.p. 110–112° (lit.[9] m.p. 104–105°), 5.7 g., λ_{max} 223, 262, 272, 282, and 294 mμ (ϵ 14,100, 8500, 11,500, 11,800, and 6,700). It was not necessary to treat dehydroergosteryl tosylate (II) with ether and it (15 g. of dried material from the potassium bicarbonate solution) could be directly recrystallized from acetone. The product from two recrystallizations weighed 11 g. and generally formed in colorless thick prisms but often needles were present. Both forms were separately investigated and found to be the same compound on the basis of their ultraviolet spectra. (See ref. 2 and 4 for the spectrum of II.) The melting point of dehydroergosteryl tosylate has been reported with various values.[1,2] In a previous investigation in this laboratory[2] the melting point of material crystallized from acetone was found to vary in the range of 103 to 113°. We have frequently obtained samples since then by the procedure described above which melted at 112–113° but which possessed ultraviolet spectra qualitatively and quantitatively identical with that reported originally. We have considered the ultraviolet absorption of either tosylate as determined in iso-octane to be the best criterion of purity.

The acetone used for recrystallizations was dried by distillation from anhydrous potassium carbonate.

Preparation of i-ergosterol (3,5-cyclo-7,22-ergostadien-6β-ol, XV). To a well stirred, boiling solution of 1.0 g. of potassium bicarbonate in 125 ml. of water and 500 ml. of acetone was added 2.0 g. of ergosteryl tosylate (XIV) which had been well ground in a mortar to insure rapid solution. The mixture was allowed to reflux for 5 min. during which time a

(18) R. Antonucci, S. Bernstein, R. Littell, K. J. Sax, and J. H. Williams, *J. Org. Chem.*, **17**, 1341 (1952).

(19) All melting points were determined on a Kofler block and are recorded as read. Analyses are by the Microanalytical Service Laboratory of this institute under the direction of Dr. William C. Alford. Rotations were taken in 1% chloroform solutions at 20° by Mrs. E. Peake. The infrared spectra were determined on a Perkin-Elmer double beam spectrophotometer (Model 21) in CS_2 by H. K. Miller with the assistance of F. L. Johnson. Ultraviolet spectra were determined on a Cary recording spectrophotometer (Model 11) with the assistance of Mrs. C. I. Wright. The ultraviolet spectra of isolated compounds were measured in an iso-octane solution unless otherwise noted, and the spectra of samples taken during kinetic experiments were measured directly against ethanol containing, appropriately, potassium acetate or oxalic acid. The ultraviolet absorption from 220 to 400 mμ of every fraction from chromatograms was determined and was the basis for combinations of fractions as well as for the evaluation of the constituents present. The elutions with a given solvent were routinely continued until the material in question no longer was being removed at a significant rate. The alumina used was purchased from M-Woelm-Eschwege, activity grade 1, and was of an acidic or basic nature as indicated. Solvents were purified, distilled, and dried with the help of J. Lyons excepting ethanol and chloroform which were the usual commercial grades of reagent material.

clear, faintly yellow solution was produced. This was distilled at atmospheric pressure until it became cloudy. Approximately 250 ml. of distillate was collected. The oily precipitate crystallized on cooling to 0°, and after being filtered and dried at 80° in a vacuum the product weighed 1.3 g. (90%) and melted at 120–122°. In the ultraviolet it showed end-absorption with ϵ 2100, 1600, and 1300 at 220, 222, and 224 mμ, respectively, as well as a maximum at 262 mμ (ϵ 790) (3% of XVI). In addition, inflections occurred near 294, 312, and 330 mμ (ϵ 50–250). The *i*-sterol was recrystallized twice from acetone and yielded 1.1 g. of colorless needles, m.p. 129–130°, $[\alpha]_D$ −11°, λ_{max} 262 mμ (ϵ 200) (0.8% XVI); end-absorption: ϵ_{220} 1,400. The highest melting point attained was 132–133°, by recrystallization of the compound from ethanol. However, recrystallization from hot ethanol did not always give satisfactory results. On occasion low melting (*ca.* 90°) samples were produced. In one instance the ethyl ether (see below) was obtained. Isooctane, dioxane, and several other solvents were tried, but acetone gave the best and most consistent results. The pure *i*-sterol (XV) (m.p. 132–133°) exhibited only end-absorption in the ultraviolet: ϵ 7400, 4900, 2300, 1300, 650, 320, 140, and 0 at 210, 214, 218, 220, 222, 224, 226 and 230 mμ, respectively, in ethanol. In the infrared it had a sharp hydroxyl band at 2.76 μ and a band of medium intensity at 6.00 μ corresponding to C=C stretching absorption. It is of interest that this double bond absorption is more intense than the absorption of 7,22-ergostadien-3β-ol which has only a weak band at 6.0 μ.

Anal. Calcd. for $C_{28}H_{44}O$ (396.6): C, 84.78; H, 11.18. Found: C, 84.74; H, 11.12.

i-Ergosteryl ethyl ether. A sample of *i*-ergosterol (m.p. 132–133°) was recrystallized from hot ethanol which, though considered to be pure, may have contained traces of acid. The colorless needles which resulted melted at 75–76°. Further recrystallization from the same ethanol or from ethanol-water failed to alter the melting point. The compound showed no O—H stretching absorption in the infrared but did exhibit strong C—O bending absorption at 9.25 μ and a band at 6.0 μ of medium intensity for C=C stretching. In the ultraviolet there was end-absorption with ϵ_{220} 2000, ϵ_{222} 1200, and ϵ_{228} 240.

Anal. Calcd. for $C_{30}H_{48}O$ (424.68): C, 84.84; H, 11.39. Found: C, 84.62; H, 11.24.

Preparation of i-dehydroergosterol (3,5-cyclo-7,9(11),22-ergostatrien-6β-ol, III). *i*-Dehydroergosterol was obtained by following exactly the same procedure as described for *i*-ergosterol except that dehydroergosteryl tosylate (II) was used in place of ergosteryl tosylate. The product which precipitated on cooling the concentrated reaction mixture was recrystallized twice from acetone and afforded III as colorless needles, m.p. 127–128°, λ_{max} 247 mμ (ϵ 16,200), in a 60% yield. The best sample prepared by the older procedure using potassium acetate as the buffer melted at 125–126° (λ_{max} 247 mμ, ϵ 16,400).[3] It is worth noting, however, that the use of potassium bicarbonate gives far superior results from the standpoint of reproducibility and ease of isolation of a pure product. Difficulties with the older procedure have not only been evident in the past but were confirmed during the course of the present work. The acid conditions produced by the potassium acetate technique yield transformation products as contaminants which are not readily separated.

Kinetic experiments. All the kinetic experiments were carried out in a constant temperature bath at 30° using commercial, absolute ethanol. The results recorded in Figures 1, 2, and 3 are typical of a number of experiments in each case.

In the solvolysis experiments 25 mg. of the tosylate (II or XIV) was dissolved in 250 ml. of ethanol containing 18 mg. of fused potassium acetate. At appropriate intervals a sample was removed and the ultraviolet absorption from 220 to 400 mμ was immediately measured directly on the sample. The logarithm of the optical density at 340 mμ for II and at 294 mμ for XIV was plotted against time (Figure 1) and the half-life (98 min. for XIV and 129 min. for II) was obtained graphically. The acid-catalyzed experiments were carried out by dissolving 10 mg. of the *i*-sterols (III or XV) in ethanol, adding 1.0 ml. of a stock solution of 450 mg. of oxalic acid in 100 ml. of water, and diluting the reaction mixture rapidly to 250 ml. with ethanol (initial concentration of steroid = 0.00010*M*). Samples were withdrawn at appropriate intervals and the ultraviolet absorption from 220 to 400 mμ was measured immediately and directly. The intensities of absorption at 247 mμ for III, 247 mμ (λ_{max} 244) for VIII, 340 mμ for X, 262 mμ for XVI, and 294 mμ for XVIII were used in the following calculations.

(A) For the reaction of *i*-dehydroergosterol (III) the extent of conversion to dehydroergosteryl ethyl ether (X) was evaluated as 80–85% by following the reaction spectrophotometrically to many times the half-life period. This agrees well with the percent conversion observed in a boiling solution under preparative conditions for X (see below). It is also in agreement with the previous[4] and present findings (see below) that the retro-*i*-steroid rearrangement of III produces 10–20% of *i*-hydrocarbon(s). The *i*-hydrocarbon (VIII) and the ethyl ether (X) both have some absorption at 247 mμ. A correction for this was made by simultaneously measuring the intensities at 247 mμ and 340 mμ. It was also observed that $\epsilon_{247}/\epsilon_{340}$ = .061 for pure X. Assuming that at any given time (t) the products are composed 18% of VIII which has an extinction coefficient of 14,200 at 247 mμ and that D^{∞}_{340} is the optical density at 340 mμ at complete reaction the following relationship was used to calculate the corrected absorption at 247 mμ for III:

$$D^{cor.}_{247} = D^{t}_{247} - \left[\frac{D^{t}_{340}}{D^{\infty}_{340}}(1.42)(0.18) + D^{t}_{340}(0.061)\right]$$

The half-life found graphically by this method was 131 min. (Figure 3).

(B) Using the same assumptions and notations as above it was possible to calculate the percent of III remaining at any given time from the concentration of the product (X). Thus:

$$\% \text{ of III remaining} = 1 - D^{t}_{340}/D^{\infty}_{340}$$

These are plotted in Figure 2. The half-life found graphically was 129 min.

(C) For the reaction of *i*-ergosterol (XV) by following the reaction spectrophotometrically to many times the half-life period it was found that D_{262}/D_{294} = 10 at all times. It was also observed from the spectrum of pure XVIII that the intensity of absorption at 262 mμ was 1.1 times the intensity at 294 mμ. The extinction coefficient of pure XVI at 262 mμ is 26,800.[11] The extinction coefficient of pure XVIII at 294 mμ is 6,900. Isolation experiments (see below) showed that XVI and XVIII were the only products. Thus, at complete reaction:

$$\frac{D^{\infty}_{262} - D^{\infty}_{294}(1.1)}{2.68} + \frac{D^{\infty}_{294}}{0.69} = 1.00$$

From these relationships it was possible to calculate the final optical density (D^{∞}_{262} = 2.1) which agreed within experimental error with that observed (2.0) and to calculate from this figure the percent conversion to XVI (70%) and to XVIII (30%). Essentially the same figures were found in the isolation experiment. Furthermore, from the final value of the optical density (D^{∞}_{262}) the percent of XV left at any given time (t) could be calculated as follows:

$$\% \text{ of XV remaining} = 1 - D^{t}_{262}/D^{\infty}_{262}$$

The results are plotted in Figure 2 and the half-life found was 198 min.

From a comparison of many experiments the half-life values quoted in this paper are considered to be accurate to within *ca.* 10%. The accuracy of the solvolysis determina-

tions is probably the highest (deviation in $t_{1/2}$ in several experiments less than 5 min.), because no corrections had to be applied and the disappearance of the starting materials could be measured directly. In the text all of the half-life values are quoted in hours so that the figures will not imply a significantly greater accuracy than is inherent in the experiments.

Acid-catalyzed reactions of i-ergosterol (XVI *and* XVIII *from* XV). A solution of 500 mg. of 3,5-cyclo-7,22-ergostadien-6β-ol (*i*-ergosterol, XV) in 50 ml. of ethanol containing 1.0 mg. of oxalic acid was refluxed for 45 min. The solution was evaporated rapidly to dryness under reduced pressure and the residue (489 mg., λ_{max} 262 and 294 mμ) was chromatographed on 15 g. of alumina ("almost neutral"). Elution with petroleum ether yielded 305 mg. (64%) of crystalline 3,5-cyclo-6,8(14)-22-ergostatriene (XVI) which was recrystallized from acetone giving 250 mg. of colorless needles, m.p. 103–104°, $[\alpha]_D$ 95°, λ_{max} 262 mμ (ε 25,900). Lit.[11] m.p. 102–102.5°, $[\alpha]_D$ 92°, λ_{max} 261 mμ (ε 26,800). Elution with chloroform yielded 132 mg. of crystalline 3β-ethoxy-5,7,22-ergostatriene (ergosteryl ethyl ether, XVIII) which was recrystallized from acetone yielding 78 mg. of microcrystals, m.p. 120–121°. Further recrystallization from ethanol raised the melting point to 123–124°, λ_{max} 262, 272, 282, and 294 mμ (ε 8000, 11,500, 12,700, and 6900), λ_{max} 9.0–9.1 μ, no OH absorption. Lit.[20] m.p. 123–124°, $[\alpha]_D$ −111°.

Acid-catalyzed reactions of i-dehydroergosterol (III). A. *Preparation of dehydroergosteryl ethyl ether* (X *from* III). A solution of 1.0 g. of 3,5-cyclo-7,9(11),22-ergostatrien-6β-ol (*i*-dehydroergosterol, III) in 100 ml. of absolute ethanol containing 2.0 mg. of oxalic acid was refluxed for 60 min. An aliquot portion was removed and analyzed spectrophotometrically. Based on the intensity of the maxima at 340 mμ and 244 mμ the conversion to dehydroergosteryl ethyl ether (X) was *ca.* 82% and to VIII 10–20%. The solution was evaporated to dryness under reduced pressure in the presence of a small amount of aqueous potassium bicarbonate and the residue was dissolved in a mixture of water and benzene. The benzene extract after being washed with aqueous potassium bicarbonate and then with water was dried and evaporated to dryness under reduced pressure. Chromatography of the residue on 30 g. of alumina ("basic") yielded some hydrocarbon by elution with petroleum ether (b.p. 30–60°). This was followed by elution with ether which yielded X from ethanol as colorless flakes, 0.33 g., m.p. 85–86°. One recrystallization afforded an analytical sample, m.p. 86–87°, $[\alpha]_D$ 197°, λ_{max} 312, 325, and 340 mμ (ε 11,300, 12,500, and 7700).

Anal. Calcd. for $C_{30}H_{46}O$ (422.67): C, 85.24; H, 10.97. Found: C, 85.41; H, 11.02.

In another experiment carried out in a similar manner from 443 mg. of III the total weight of pure X was 208 mg. (65%) obtained from ether eluates, of *i*-hydrocarbon (principally VIII by ultraviolet) 46 mg. (11%) obtained from petroleum ether eluates, and of a mixture (ultraviolet) of these 63 mg. (15%) by stripping the column with chloroform. The ultraviolet spectrum of the 46 mg. of *i*-hydrocarbon differed from pure VIII in that there was a more pronounced inflection at *ca.* 252 mμ, the minimum near 261 mμ was of much higher intensity and the maximum at 295 mμ was only about half the intensity of that at 244 mμ, while normally it is 74% as intense.

B. Rearrangement and retrorearrangement without isolation of i-dehydroergosterol (X *from* II *and* I *from* II). A solution of 200 mg. of dehydroergosteryl tosylate (II) in 20 ml. of ethanol was refluxed for 10 min. in the absence of a buffer. To this was then added 146 mg. of potassium bicarbonate and the ethanol was removed by vacuum distillation. The residue was chromatographed as described in A. The ether (X) was crystallized from ethanol yielding flakes, m.p. 69–72°, λ_{max} 312, 324, and 340 mμ (ε 7900, 9000, and 5600), of 73% purity.

When a similar reaction was carried out for *ca.* 10 min. in aqueous acetone instead of ethanol the product was isolated without chromatography. From 200 mg. of dehydroergosteryl tosylate (II) there was obtained 110 mg. of dehydroergosterol (I), m.p. 101–110°, λ_{max} 244, 312, 324, and 340 mμ (ε 1600, 8000, 9000, 5690), of 77% purity.

The reaction of dehydroergosteryl tosylate in ethanol or aqueous acetone in the absence of a buffer produces a strongly acid reaction mixture. Such conditions are favorable for the product (X or I) to undergo the anthrasteroid rearrangement[3] and probably explains why the chromatographed ether from procedure B was only 73% pure. The reactions of I and X under strongly acid conditions in hydroxylic solvents as well as in chloroform comprise the subject of another investigation which will be reported on shortly. The preparation of dehydroergosteryl ethyl ether (X) from dehydroergosterol is best carried out *via* the pure *i*-sterol (III) as described in A. This appears to be the only method reported for converting dehydroergosterol into its 3-ethers. The preparation of the methyl ether was achieved by Heilbron and Simpson,[20] but these authors first made the methyl ether of ergosterol. This was then dehydrogenated with mercuric acetate.

3,5-Cyclo-6,8(14),22-ergostatriene (XVI) *from ergosteryl tosylate* (XIV) *in pyridine.* A hot solution of ergosteryl tosylate (2.0 g.) in 20 ml. of hot pyridine was maintained at 100° for 17 min. and was then evaporated to dryness under reduced pressure. The residue was extracted with two 100-ml. portions of boiling petroleum ether (b.p. 30–60°) and after filtration the solvent was removed at reduced pressure. The crude product (λ_{max} 262 mμ, ε 15,700; λ_{infl} 290–296 mμ, ε 1500) was crystallized from acetone and yielded 0.77 g. (56%) of XVI, m.p. 94–97°, which was further purified by chromatography on alumina ("almost neutral"). The residue from eluates of petroleum ether (b.p. 30–60°) was crystallized from acetone and yielded 503 mg. of the *i*-hydrocarbon (XVI) as long, colorless prisms, m.p. 102–103°, λ_{max} 262 mμ (ε 24,200), λ_{infl} 290–296 mμ (ε 1300). Lit.[11] m.p. 102–102.5°, $\lambda_{max}^{alc.}$ 261 mμ (ε 26,800). (Cf. XVI from XV.) Fieser, Rosen, and Fieser[11] have reported that dehydration of ergosterol by various procedures yields not only XVI but another hydrocarbon which is isomerized to XVI by heat or acid-washed alumina. Based on the presence of an inflection near 293 mμ in our crude and chromatographed materials it is possible that their second hydrocarbon as well as our contaminant (<10% of our purified product) is the isomer (XVII) with a 6,8-diene system which could originate by elimination of a proton at C-9. Such a homoannular diene system conjugated with a cyclopropyl ring would give rise to a band near 290 mμ, and should isomerize to the more stable heteroannular diene system as in XVI. Still a third contaminant, especially in our crude product, is possible, *viz.*, a compound with an unconjugated diene system as has been reported from dehydrohalogenation of 7-bromocholesterol in pyridine.[21]

Reaction of dehydroergosteryl tosylate with pyridine. A solution of 2.0 g. of dehydroergosteryl tosylate in 20 ml. of hot pyridine was heated at 100° for 30 min. The solution was then evaporated to dryness under reduced pressure and the residue was extracted with four 50-ml. portions of boiling petroleum ether (b.p. 30–60°). A large portion (1.95 g.) of the solid residue failed to dissolve and was not investigated further. The petroleum ether extract was concentrated and adsorbed on a column of alumina ("almost neutral") and elution with the same solvent yielded, after crystallization from acetone, 39 mg. (3%) of slightly impure *i*-hydrocarbon (VIII), m.p. 90–93°, λ_{max} 244 and 295 mμ (ε 14,500 and

(20) I. M. Heilbron and J. C. E. Simpson, *J. Chem. Soc.*, 268 (1932).

(21) K. Tsuda, K. Arima, and R. Hayatsu, *J. Am. Chem. Soc.*, **76**, 2933 (1954); see also W. R. Nes, R. B. Kostic, and E. Mosettig, *J. Am. Chem. Soc.*, **78**, 436 (1956).

10,200). Lit.[2] m.p. 98–100°, λ_{max} 244 and 295 mμ (ε 16,300 and 11,700).

Several similar reactions were carried out for various periods ranging up to 4 hr., but in every case the total extractable (petroleum ether) material amounted to not more than *ca.* 15% of the original weight of starting material.

Preparation of 3,5-cyclo-6,8(14),9(11),22-ergostatetraene (VIII *from* III). A solution of 1.0 g. of *i*-dehydroergosterol (III) (m.p. 126–127°) and 1.0 ml. of trichloroacetyl chloride in 20 ml. of pyridine was allowed to stand overnight at room temperature. The resulting red solution was poured into a mixture of ice and aqueous potassium bicarbonate and the oily product was extracted into chloroform. The chloroform solution was washed, dried, and evaporated to dryness. Chromatography on 30 g. of alumina ("almost neutral") and elution with petroleum ether (b.p. 30–60°) yielded 0.4 g. of the hydrocarbon which after crystallization from acetone-water was still only 92% pure (λ_{max} 244 and 295 mμ, ε 15,000 and 11,000). The pure material was obtained by recrystallizing it twice further from acetone-methanol and gave VIII as colorless, long rods, m.p. 99–101°, λ_{max} 244 and 295 mμ (ε 16,100 and 12,100). Lit.[3] m.p. 98–100°, λ_{max} 244 and 295 mμ (ε 16,300 and 11,700). Elution of the chromatographic column with chloroform gave 88 mg. of dehydroergosterol (I), identified on the basis of its ultraviolet spectrum.

The hydrocarbon (VIII) was also obtained from the reaction of *i*-dehydroergosterol and 3,5-dinitrobenzoyl chloride in pyridine. However, both the reaction of *i*-dehydroergosterol with benzoyl chloride and with *p*-nitrobenzoyl chloride yielded products with ultraviolet spectra consistent with the corresponding 3,5-cyclo steroid ester and hydrolysis of these with hot potassium bicarbonate in aqueous acetone gave back the starting material.

An attempt to prepare and isolate the trichloroacetate of *i*-dehydroergosterol by the reaction (15 min. at room temp.) of *i*-dehydroergosterol in benzene containing 2 equivalents of pyridine and 1 equivalent of trichloroacetyl chloride followed by extraction with a cold aqueous potassium bicarbonate solution yielded an oil exhibiting maxima at 244, 295, 311, 324, and 340 mμ with approximately the same intensities at 244 and 324 mμ. On slow evaporation of the mixture from methanol-water crystals were obtained which showed substantially the same spectrum. The intensities of the maxima indicated a 40% content of I and a 40% content of VIII.

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BETHESDA 14, MD.

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH PUBLIC HEALTH SERVICE, U. S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE]

Ribofuranose Derivatives from 3,5-Di-*O*-benzoyl-D-ribosyl Chloride. I. 1,3,5-Tri-*O*-benzoyl-β-D-ribose and 5-*O*-Benzoyl-1,2,3-*O*-benzylidyne-α-D-ribose*[1]

ROBERT K. NESS AND HEWITT G. FLETCHER, JR.

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Condensation of the crystalline furanosyl halide, 3,5-di-*O*-benzoyl-D-ribosyl chloride (II), in ether solution with silver benzoate gives, in addition to the previously known 1,3,5-tri-*O*-benzoyl-α-D-ribose (I), a new D-ribofuranose tribenzoate which is shown to be 1,3,5-tri-*O*-benzoyl-β-D-ribose (III). Treatment of the same halide (II) in benzene solution with mercuric acetate gives a mono-*O*-benzoyl-*O*-benzylidyne-D-ribose which, by a series of reactions, has been converted to 1,2,3-tri-*O*-benzoyl-5-*O*-methanesulfonyl-β-D-ribose (XII). Synthesis of the latter substance from the known 2,3-*O*-benzylidene-β-D-ribofuranose (XIII) confirmed its structure and led to the conclusion that the orthoester is 5-*O*-benzoyl-1,2,3-*O*-benzylidyne-α-D-ribose (VII).

The nature of the crystalline halide (II) is discussed with particular reference to the question of its anomeric configuration.

In recent communications we have described the preparation of 3,5-di-*O*-benzoyl-D-ribosyl bromide[4] and 3,5-di-*O*-benzoyl-D-ribosyl chloride (II).[5] These two substances are of unusual interest not only because they are the first ribofuranosyl halides to be obtained in crystalline form[6] but also because they are readily accessible from D-ribose[4] or from 2,3,5-tri-*O*-benzoyl-D-ribose[7] and, therefore, are of potential value for the synthesis of ribonucleosides. While both of these halides are relatively labile substances the chloride is, as might be expected, somewhat less reactive than the bromide and is, therefore, a more convenient object of study from the experimental point of view. The present paper will be devoted primarily to a description of the preparation, characterization, and proof of structure

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* This paper is a contribution in honor of Lyndon F. Small, former Editor of the Journal.

(1) In earlier papers (refs. 2 and 3) dealing with derivatives of orthobenzoic acid we have used the prefix "orthobenzoyl" to refer to the radical $C_6H_5C{\equiv}$. In the present and following papers we adopt the more accurate prefix "benzylidyne"; *cf. Chem. Abstr.*, **39**, 5963 (1945).

(2) H. G. Fletcher, Jr., and R. K. Ness, *J. Am. Chem. Soc.*, **77**, 5337 (1955).

(3) R. K. Ness and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **78**, 1001 (1956).

(4) R. K. Ness and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **76**, 1663 (1954).

(5) R. K. Ness and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **78**, 4710 (1956).

(6) One more crystalline di-*O*-benzoyl-D-ribofuranosyl halide is reported in the communication immediately following this one.

(7) R. K. Ness, H. W. Diehl, and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **76**, 763 (1954).