approximately 92 kcal. and represents a maximum value of the activation energy, since some of the energy absorbed may be dissipated as heat.

We have considered many mechanisms for this rearrangement and the value which we calculate for the transformation involving the lowest activation energy is 72 kcal. The mechanism of this rearrangement will be described in some detail.

Initially the carbon atoms 1, 2 and 3 and the hydrogen atom taking part in the reaction are in the same plane. The C–H group rotates about the 1,3-carbon–carbon bond until the three carbon atoms are at the corners of an equilateral triangle with the hydrogen atom equidistant (approximately 1.12 Å.) from carbon atoms 2 and 3. Up to this point all four atoms remain in the same plane. The next three steps occur simultaneously: (1) the hydrogen atom moves away from carbon atom 3, at the same time maintaining a constant distance from carbon atom 2; (2) carbon atoms 1 and 2 separate to a distance of approximately 2.07 Å.; and (3) the two parts of the molecule formed by the breaking of the 1,2-carbon–carbon bond rotate about the 5,6-carbon–carbon bond so that the plane of carbon atoms 2, 6 and 7 is at an angle of approximately 26° with that of the carbon atoms 1, 4 and 5. Following these steps the hydrogen atom moves to a final position determined by the ring of which carbon atom 2 is a part, and by the valence angles of this carbon atom. The system is now in the activated state and from this point onward (that is, as the rotation about the 5,6-carbon–carbon bond continues) the energy of the system decreases.

There are two factors which we have not considered that will affect the energy required for activation. The double bond which is formed between carbon atoms 1 and 3 is part of a conjugated system (atoms 3,1,4,5,6,7) and, although quantitative calculations have not been made, we know that this will tend to lower the activation energy slightly. The large size of the molecule introduces steric factors which probably will cause an increase in the activation energy. These two factors will tend to cancel each other, and we have not attempted to estimate them quantitatively. Their effect will not be large.

From the nature of the rearrangement it is evident that another mechanism could involve the breaking of a C–H bond (92.3 kcal.) and a reaction of the H atom with carbon atom number 2. This mechanism would therefore involve an energy of 92.3 kcal., and hence we conclude that the activation energy for the conversion of ergosterol to calciferol lies between 72 and 92 kcal. This is consistent with the value found by Steenbock for the long wave length limit.

One of us (A. S.) wishes to acknowledge support from the Wisconsin Alumni Research Foundation and the other gratefully acknowledges support from the Phi Kappa Phi honor society.

PHYSICAL CHEMICAL LABORATORY
UNIVERSITY OF WISCONSIN
MADISON, WISCONSIN RECEIVED JANUARY 13, 1937

A Simple Method for the Preparation of the Chloro Ketone $C_{19}H_{27}OCl$, Dehydroandrosteryl Chloride

BY EVERETT S. WALLIS AND E. FERNHOLZ

In a recent paper by A. Butenandt and W. Grosse[1] the statement is made that replacement of the hydroxyl group in dehydroandrosterone by chlorine by the usual methods is unsatisfactory, low yields of the chloro ketone being obtained. From what is written one gets the impression that the difficulties involved are, indeed, serious, for the authors considered other possibilities and developed a new method which involves the following steps

Dehydroandrosterone ⟶ toluenesulfonate (71%) ⟶ *epi*-dehydroandrosterone methyl ether[2] (99%) ⟶ dehydroandrosteryl chloride (79%); yield over all (56%)

As is readily seen the yield of the chloride is not too satisfactory and even if we could consider the yield as fair the method would still be involved.

In the course of some of our experiments we have had occasion also to prepare this important chloro ketone. In our hands the treatment of dehydroandrosterone with phosphorus pentachloride has always given very satisfactory results. When the reaction is carried out in chloroform solution the yield is 83%, and the preparation involves but one step.

Experimental Part

One gram of dehydroandrosterone was added to a mixture of 10 cc. of dry chloroform and 1 g. of phosphorus

(1) A. Butenandt and W. Grosse, *Ber.*, **69**, 2776 (1936).

(2) The experimental results of Wallis, Fernholz and Gephart [THIS JOURNAL, **59**, 137 (1937)] obtained in a study of the action of potassium acetate on cholesteryl *p*-toluene-sulfonate show that a molecular rearrangement takes place during this reaction. In the light of these experiments the naming of this methyl ether may not be justified. It is entirely possible that the compound may have a different structure.

pentachloride. A violent reaction took place. The resulting mixture was kept at room temperature for one hour. Water was then added (100 cc.), the two layers were separated, and the chloroform layer removed to the steam-bath. During the evaporation of the chloroform the chloride crystallized. It was filtered and dissolved in ether. The ether solution was washed with sodium hydroxide to remove acidic esters. The ether residue after one crystallization gave an almost pure chloride; yield 0.76 g.; m. p. 153°. The mother liquor was evaporated and the residue was distilled in high vacuum and recrystallized from methyl alcohol; yield 0.12 g.; total yield 0.88 g. (83%). Further repeated recrystallizations did not raise the melting point above 154° (uncorr.); $[\alpha]^{22}D$ +14.6° (19.2 mg. in 2 cc. of chloroform solution gave $\alpha^{22}D$ +0.14°, 1-dm. tube).

Summary.—A simple method is described for the preparation of dehydroandrosteryl chloride in good yield. The chloro ketone so prepared melts at 154° and has a specific rotation $[\alpha]^{22}D$ +14.6°.

FRICK CHEMICAL LABORATORY
PRINCETON UNIVERSITY
PRINCETON, N. J. RECEIVED JANUARY 28, 1937

The Separation of the C_{17}-Epimers of Oestradiol by Digitonin

BY O. WINTERSTEINER

It has been shown by Schwenk and Hildebrandt[1] that two epimeric forms of oestradiol can be obtained by catalytic reduction of the 17-keto group of oestrone (theelin). The lower melting α-isomer (m. p. 178°, $[\alpha]D$ +81°), which occurs in follicular fluid[2] and in the urine of pregnant mares,[3] is the most potent oestrogenic compound known. The higher melting β-isomer (m. p. 223°, $[\alpha]D$ +54°), which is much less active physiologically, has only recently been prepared in pure form. Its properties will be described in more detail in a separate communication.[4] We have found recently that the two isomers can be separated conveniently by digitonin, whereby the laborious separation by fractional crystallization may be avoided. Only the lower-melting α-isomer forms a sparingly soluble digitonide, when treated with a solution of digitonin in 80% alcohol. The molecular compound deposits slowly in form of beautiful needles, which melt at about 265° after partial decomposition at 195°, and from which the diol can be regenerated easily by the usual methods. Also the 3-benzoate of the α-isomer yields a crystalline precipitate with digitonin, though more slowly than the free diol. Neither the high melting β-oestradiol nor its 3-benzoate precipitates with digitonin under identical conditions. These results show clearly that it is the configuration of the 17-carbon atom which determines the capacity to form insoluble digitonides of this type.

The digitonin reaction is also negative with oestriol (theelol), dihydroequilenin (δ-follicular hormone)[5] and 17-*trans*-testosterone.[6] Furthermore, no precipitate was obtained with a crude preparation of androstenediol-3-acetate, which according to the mode of its preparation should have contained some of the 17-*cis*-epimer. The melting point of dihydroequilenin, and that of its benzoate, its low specific rotation ($[\alpha]D$ −4.7°), its low physiological potency, and its failure to precipitate with digitonin would place this compound in the β-series of oestrogenic diols. On the other hand, if the same criteria be applied to 17-*trans*-testosterone, all the data except the negative digitonin reaction speak for its steric relationship to α-oestradiol. Caution is obviously necessary in interpreting the behavior of C_{17}-epimers toward digitonin as an indication of stereochemical relationships.

In the pregnane series, Butenandt and coworkers[7] have employed digitonin for the separation of C_{17}-epimers. *allo*-Pregnanedione, *allo*-pregnanol-3-one-20-3-acetate, and Δ^5-pregnenol-3-one-20, but not their C_{17}-epimers, termed *iso*-compounds by these workers, form insoluble digitonides.

(1) Schwenk and Hildebrandt, *Naturwiss.*, **21**, 177 (1933).
(2) MacCorquodale, Thayer and Doisy, *Proc. Soc. Exptl. Biol. Med.*, **32**, 1182 (1935); *J. Biol. Chem.*, **115**, 435 (1936).
(3) Wintersteiner, Schwenk and Whitman, *Proc. Soc. Exptl. Biol. Med.*, **32**, 1087 (1935).
(4) Whitman, Wintersteiner and Schwenk, forthcoming publication.
(5) Wintersteiner, Schwenk, Hirschmann and Whitman, THIS JOURNAL, **58**, 2652 (1936).
(6) Ruzicka and Kägi, *Helv. Chim. Acta*, **19**, 842 (1936).
(7) Butenandt and Mamoli, *Ber.*, **68**, 1847 (1935); Butenandt and Fleischer, *ibid.*, **70**, 96 (1937).

DEPARTMENT OF BIOLOGICAL CHEMISTRY
COLUMBIA UNIVERSITY
NEW YORK, N. Y. RECEIVED JANUARY 28, 1937

Reaction of Lanthanum Oxide with Ammonium Iodide

BY RALPH C. YOUNG AND JANE L. HASTINGS

By following the general method of Reed, Hopkins and Audrieth[1] for the preparation of the chlo-

(1) Reed with Hopkins and Audrieth, THIS JOURNAL, **57**, 1159 (1935).