nicht aufzählen kann, getragen haben, kann nur aus dem Buche selbst deutlich ersehen werden. Diese Forscher haben nachgewiesen, daß der säkulare Gang der Erdbestrahlung, wie er mit den Strahlungstabellen und durch meine Strahlungskurven veranschaulicht wurde, deutliche Spuren im Alpengebiet hinterlassen und durch die bei den einzelnen Gletschervorstößen geschaffenen Erdmoränen seine Ausschläge und seinen Rhythmus derart markiert hat, daß eine weitgehende Zergliederung und eine auf zuverlässiger astronomischer Berechnung fußende Chronologie des alpinen Glazials aufgestellt werden konnte.

Dies gilt, vielleicht in noch größerem Maße, für das Randgebiet der norddeutschen Vereisungen. Hier haben die Terrassen der Flüsse alle Ausschläge der Strahlungskurven deutlich markiert, so daß nicht nur die neun großen Ausschläge, sondern auch die kleineren ihr Korrelat in den Schotterterrassen dieser Flüsse fanden.

Aus dieser Zusammenstimmung unternahmen es deutsche Geologen, namentlich SÖRGEL und seine Schüler, zur Vollgliederung des Eiszeitalters zu schreiten und dehnten dabei ihre Untersuchungen auf das übrige Europa aus; russische, polnische, finnländische, italienische und ungarische Forscher beteiligten sich an diesem Unternehmen.

Seit der Fertigstellung des *Kanons*[1] habe ich, isoliert von der übrigen Welt, den soeben geschilderten Aufschwung nicht weiter verfolgen können.

Summary

After numerous attempts to explain the phenomenon of the glacial periods, undertaken since 1842, had failed, it became evident that the solution of this problem must be sought in a wider field of science. When finally use was made of the requisite items of knowledge concerning celestial mechanics, spheric astronomy, and cosmic rays, the secular variations of the terrestrial radiation could be calculated exactly out of their interrelations, which gave the key to the solution. How this came about is described in detail in the article.

[1] Im Klimaheft der «Geologischen Rundschau» (1943) teilten W. WUNDT und W. MEINARDUS die Ergebnisse der *Kanons* mit und widerlegten anhand derselben Einwände gegen meine Theorie der Eiszeiten.

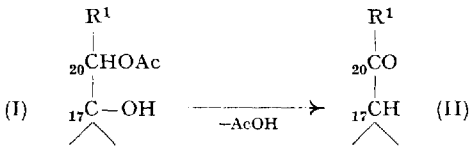
ADDITAMENTUM

ad L. FIESER et M. FIESER, Exper. *4*, 285 (1948)

The Serini Reaction

By C.W. SHOPPEE[1], London

This reaction, discovered by SLOTTA and NEISSER[2], and first employed in the steroid field by SERINI *et al.*[3], involves the conversion of a 17:20-diol 20-acetate (I) by treatment with zinc dust into a 20-ketone (II). It has recently been discussed by FIESER and FIESER[4] who give a concise and valuable summary of the available examples.



There is no direct evidence as to the mechanism of the Serini reaction and FIESER and FIESER[4] postulate that an enol-acetate, a 17:20-oxide, or a cyclic orthoester is formed as an intermediate by *trans*-elimination or cyclisation. On the basis of the stereochemical form (C_{13}-Me/C_{20}-R^1: *cis* or *trans*) of such an intermediate, they achieve an empirical correlation of the existing data, and are able to account for the production through a *trans*-intermediate of the 17-*iso*-20-ketone (IV) from *both* the 17*n*-20b-acetate (III) and the 17-*iso*-20a-acetate (V)[1].

On the same stereochemical basis, however, FIESER and FIESER predict that REICHSTEIN'S substance 0-diacetate (*allo*pregnane-3β:17α:20a-triol diacetate[2])

[1] The Chester Beatty Research Institute, The Royal Cancer Hospital, University of London, and University College, Swansea.

[2] K. H. SLOTTA and K. NEISSER, Ber. Dtsch. chem. Ges. *71*, 2342 (1938).

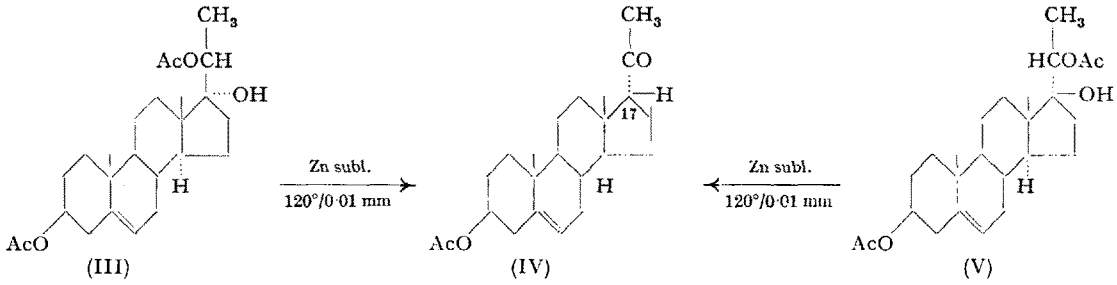
[3] A. SERINI, W. LOGEMANN, and W. HILDEBRAND, Ber. Dtsch. chem. Ges. *72*, 391 (1939).

[4] L. F. FIESER and MARY FIESER, Exper. *4*, 285 (1948).

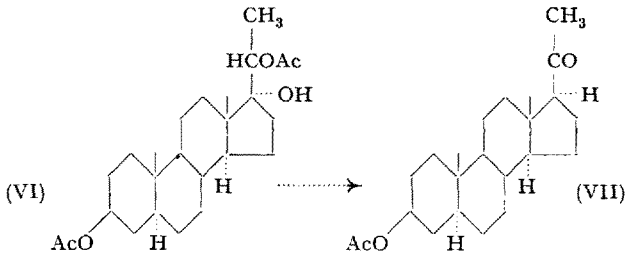
[1] A. BUTENANDT, J. SCHMIDT-THOMÉ, H. PAUL, Ber. Dtsch. chem. Ges. *72*, 1112 (1939).

[2] The nomenclature proposed by FIESER and FIESER (*loc. cit.*), with a view to international adoption is used here and supersedes that formerly employed by the writer:—"α" and "β" remain as trivial indices; (α) and (β), denoting orientation of nuclear substituents, become α and β, and their use is extended to C_{20} *only* in the side-chain for configurations which can be related to configuration at C_{17} in accordance with the convention suggested by FIESER and FIESER; α and β, denoting configuration in the side-chain, become a and b, e. g. for configuration at C_{20} non-relative to C_{17}, as in the pregnane-3:20-diols, and at C_{22} in the phytosterols.

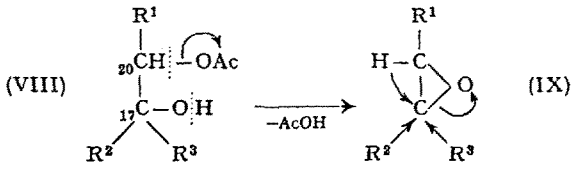
This system eliminates the stereochemical use of parentheses but maintains the distinction which they signified; it can therefore be used in respect of continental nomenclature e. g. androstandiol-(3α,11β)-on-17 in which the parentheses were and still are used only typographically.



(VI) should undergo the Serini reaction to give, through a *cis*-intermediate, *allo*pregnane-3β-ol-20-one acetate (VII) with preservation of configuration at C_{17}:



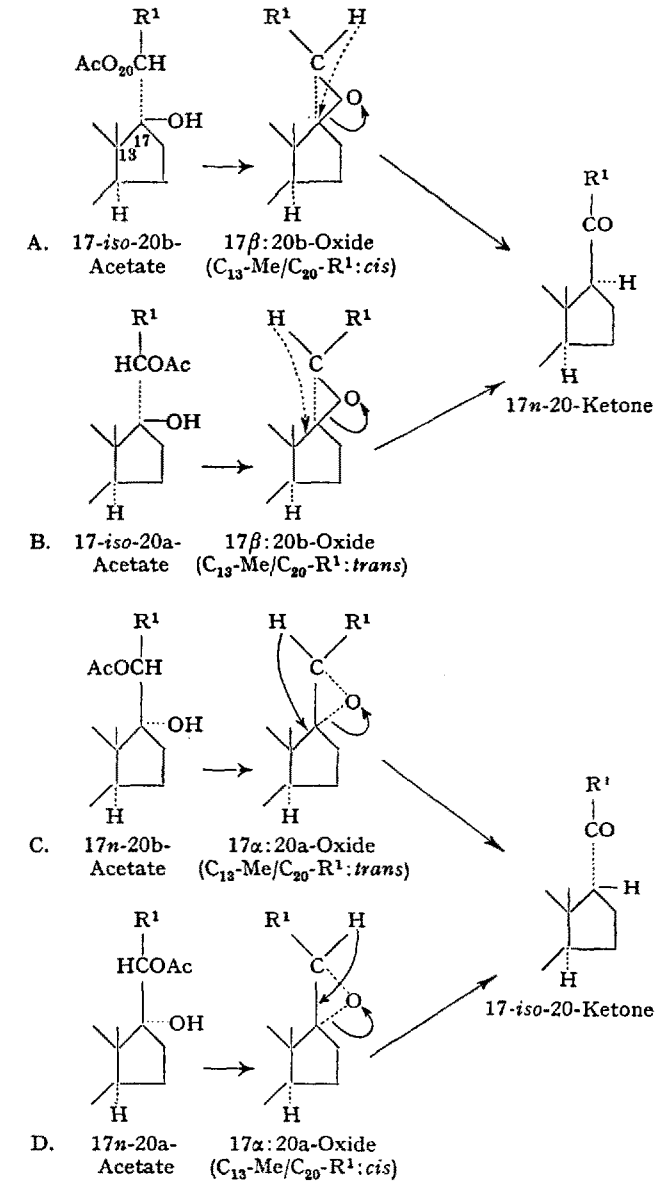
The present writer regards the Serini reaction as an example of pinacolic electron displacement[1]. The first stage of the reaction is the separation of an acetate ion from the 20-acetate (VIII) which is consistent with the tendency, OAc>OH, of anionisation. The resulting oxide (IX) then undergoes pinacolic rearrangement, many examples of which are known, and the direction of which depends on the relative electron release capacities of the groups R^1, R^2, R^3 [2]. In the case of steroid 17:20-oxides, usually $R^1 = CH_3$ or CH_2OAc, whilst $R^2 = \begin{matrix} C_8 \\ C_{12} \\ C_{14} \end{matrix}\!\!>\!C_{13}-$ and $R^3 = \begin{matrix} C_{13} \\ C_8 \end{matrix}\!\!>\!C_{14}\cdot C_{15}\cdot C_{16}-$ i.e. R^2 and R^3 are higher alkyl groups with electron release capacities greater than that of the methyl group, so that the direction of rearrangement clearly must be that depicted in (IX), whereby the electron pair constituting the C_{17}-O bond leaves the octet of C_{17} with a sextet; this gives $C_{17}\oplus$ to which the C_{20}-hydrogen migrates with its electron pair.



The factors which determine the stereochemical result of the pinacolic rearrangement depicted in (IX) are the geometry of the transition state and the orientation of the oxide ring.

In general a transition state of linear type $X\ldots\overset{|}{\underset{\wedge}{C}}\ldots Y$ is intrinsically more probable than one of pyramidal type $C\begin{matrix}\cdots X \\ \wedge \\ \cdots Y\end{matrix}$; in the present instance the formation of a linear transition state has as its inevitable consequence inversion of configuration at C_{17}.

In the *formation* from (VIII) of the oxide (IX), the C_{17}-O bond remains unbroken and will retain its original orientation; two types arise according as the



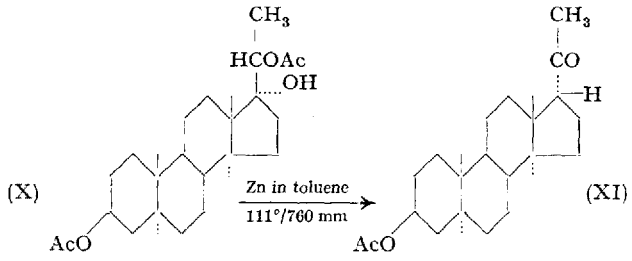
The dotted arrows from the C_{20}-H to C_{17} indicate attack at the rear face of C_{17}; the full-line arrows from the C_{20}-H to C_{17} indicate attack at the front face of C_{17}.

[1] C. W. SHOPPEE, Proc. Leeds. Lit. Phil. Soc. *1*, 301 (1928).
[2] C. K. INGOLD, Ann. Rep. Chem. Soc. *25*, 135 (1928).

oxide is a 17β:20b-oxide or a 17α:20a-oxide. Although as will be shown, contrary to the suggestion of FIESER and FIESER[1], the orientation of the hydrogen atom (or conversely the orientation of the group R[1]) attached to C_{20} in (IX) is not a factor in the situation, 4 cases must be considered according as the original compound (VIII) is a 20b-acetate or a 20a-acetate.

Case A is exemplified by the original example of SERINI *et al*[2]., whereby 17-*iso*pregn-4-ene-17β:20b:21-triol-3-one diacetate gives 11-deoxycorticosterone acetate with inversion at C_{17}. Case B should be represented by the rearrangement of 17-*iso*-pregn-5-ene-3β:17α:20a-triol diacetate; BUTENANDT *et al.*[3] describe in detail the rearrangement of this substance *or* its 17*n*-20b-isomeride (Case C) to 17-*iso*pregnenolone acetate, but it is impossible to tell from the text which isomeride was actually used. They say, however:—"Man kann zur Abspaltung von Essigsäure beide Isomeren oder auch ihre Mischung verwenden und erhält in jedem Fall das gleiche Reaktionsprodukt." The production from the 17-*iso*-20a-isomeride of a 17-*iso*ketone, i.e., with retention of configuration at C_{17}, is anomalous, and is being re-investigated by Dr. MINLON-HUANG in Prof. FIESER's laboratory. Case C is illustrated by three well established examples; the conversion of Substance A triacetate to Substance 17-*iso*R diacetate[4], of *allo*pregnane-3β:17α:20b:21-triol-11-one triacetate to Substance 17-*iso*N diacetate[4], and of pregn-4-ene-17α:20b:21-triol-3-one diacetate to 17-*iso*-11-desoxycorticosterone acetate[5]. If BUTENANDT *et al.*[3] actually used pregn-5-ene-3β:17α:20b-triol diacetate in the production of 17-*iso*-pregnenolone acetate, this would constitute a fourth example.

There is no known example of case D, but with the kind co-operation of Prof. REICHSTEIN, who most generously provided 100 mg of Substance 0-diacetate, this case has now been examined. By treatment with zinc dust in boiling toluene, Substance 0-diacetate (X) gives a 45% yield of 17-*isoallo*pregnan-3β-ol-20-one acetate (XI), m. p. 118°, $[\alpha]_D$ −73° (Found: C, 76·65; H, 9·97. Calc. for $C_{23}H_{36}O_3$ (360·52): C, 76·62; H, 10·06%). This acetate is identified as a 17-*iso*-compound beyond all doubt by its relatively large *lævo*rotation; the previous specimen prepared by BUTENANDT and MAMOLI[1], m. p. 101°, no rotation determined, contained a serious proportion of the 17-*n*-acetate, m. p. 144°, $[\alpha]_D$ +77° ($CHCl_3$)[2], as judged by the molecular rotatory powers of the parent 17-*iso*ketol, m.p. 148°, $[\alpha]_D^{19}$ +6° (EtOH)[3], $[M]_D$ +19°, and the 17-*n*-ketol, m. p. 194°, $[\alpha]_D^{19}$ +91° (EtOH)[1], +96° ($CHCl_3$)[2], $[M]_D$ ~ +300°. The molecular rotation difference for the inversion C_{17}-*normal* → C_{17}-*iso* is known to be ~ −500°, so that the pure 17-*iso*ketol should possess $[M]_D$ ~ −200° and $[\alpha]_D$ ~ −63°; $[\alpha]_D$ for the pure 17-*iso*ketol acetate should not differ greatly from the value for the free ketol, namely −63°, which is in good agreement with that now found experimentally.



This experimental result substantiates the theoretical expectation of inversion of configuration at C_{17}, and supports the view here developed of the mechanism of the Serini reaction. A full account will appear in the "Journal of the Chemical Society" in due course.

It is a pleasure again to acknowledge the gift by Prof. REICHSTEIN of 100 mg of Substance 0 diacetate, and to thank Prof. and Mrs. FIESER for a copy of the MS. of their paper[5].

Zusammenfassung

Der Mechanismus der Serini-Reaktion wird kurz erörtert und ein 17,20-Oxyd als Zwischenprodukt vorgeschlagen. Das stereochemische Ergebnis der Reaktion soll von zwei Faktoren abhängig sein, und zwar: 1. von der Geometrie des «transition state» und 2. von der Konfiguration des Oxydrings. Ausgehend von diesen Überlegungen, kann vorausgesagt werden, daß REICHSTEINS Substanz 0-Diacetat durch die Serini-Reaktion in ein 17-*Iso*-20-keton und nicht in ein 17-*Normal*-20-keton umgewandelt werden soll. Tatsächlich ist das 17-*Isoallo*pregnanol-(3β)-on-20 als einziges Produkt experimentell aufgefunden worden.

[1] L. F. FIESER and MARY FIESER, Exper. *4*, 285 (1948).
[2] A. SERINI, W. LOGEMANN, and W. HILDEBRAND, Ber. Dtsch. chem. Ges. *72*, 391 (1939).
[3] A. BUTENANDT, J. SCHMIDT-THOMÉ, and H. PAUL, Ber. Dtsch. chem. Ges. *72*, 1112 (1939).
[4] C. W. SHOPPEE and T. REICHSTEIN, Helv. chim. acta *23*, 729 (1940).
[5] C. W. SHOPPEE, Helv. chim. acta *23*, 925 (1940).

[1] A. BUTENANDT, and L. MAMOLI, Ber. Dtsch. chem. Ges. *68*, 1847 (1935).
[2] D. H. R. BARTON, private communication.
[3] A. BUTENANDT, J. SCHMIDT-THOMÉ, and H. PAUL, Ber. Dtsch. chem. Ges. *72*, 1112 (1939).
[4] M. STEIGER and T. REICHSTEIN, Helv. chim. acta *21*, 546 (1938).
[5] L. F. FIESER and MARY FIESER, Exper. *4*, 285 (1948).