auffälligen Eigenschaften. Dies Gehirn war erheblich umfangreicher als das von Eohippus, und zwar vorwiegend durch das Volumen der Oblongata; deren beide Durchmesser am Foramen magnum sind das Vierfache von *Hyracotherium*, und damit liegen sie in der Variationsbreite von *Equus*. Das Großhirn war anscheinend nicht gefurcht, und es ist zwar doppelt so breit als das von Eohippus, aber es ist nur $^1/_3$ höher und $^1/_3$ länger – d.h. es war ein geradezu winziger Teil des Gesamthirns. Der Ausguß der Sella turcica ist, wie die Hypophyse beim Pferd – aber nicht bei dessen kleineren Ahnen – herzförmig; der Vorderlappen der Hypophyse dieses *Haplolambda* (?) war fast halb so breit als sein Großhirn! – Hier hatte sich also die Anwendung von Ergebnissen der Pferdestudie als richtig erwiesen. Aber die Paläoneurologie beginnt ja eben erst mit solcherlei Forschung. Neues Material wird nicht nur unsere Kenntnis wirklich phylogenetischer Entwicklung der Gehirne erweitern, sondern auch den Geltungsbereich im Augenblick scheinbar gesicherter Ergebnisse einschränken.

Summary

The material of paleoneurology has been assembled more or less by chance. Representing a random assortment of brains of various fossil vertebrates from different geological horizons, it was not a reliable basis for that special task of paleoneurology, the study of brain evolution through the ages. A new phase began for paleoneurology when the collaboration of American museums resulted in the preparation of endocranial casts from almost every stage of the well-established evolutionary history of the horse. Now it was possible to follow the evolution of a brain through a period of about 55 million years. In the gradual transformation of the *Hyracotherium* brain into that of *Equus* the main feature was found to have been greater expansion of cerebrum, neopallium and corresponding portion of the cerebellum than of the other brain portions. Comparison of the brains today characteristic of lower placental mammals with those today characteristic of the higher forms had suggested that this is the main trend in progressive brain evolution, However, *Hyracotherium* (and other early Tertiary representatives of the higher, specialized eutherian orders) had a brain which had not yet reached the evolutionary level of even the most primitive of Recent eutherian brains. The characteristics of the *Equus* brain were not present in the Equidæ for the greater part of this family's history. In their gradual development, the equid brain passed through evolutionary stages which are not represented in the series of Recent mammal brains, until about 15 million years ago it reached the Recent level of ungulate brain evolution. The various results of this one investigation indicate that more studies of such phyletic brain histories will reveal further, still unknown data on brains and on evolution in general, facts of a kind which only a purposeful paleoneurology can furnish.

Brèves communications - Kurze Mitteilungen Brevi comunicazioni - Brief Reports

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Mechanism of the Photocondensation of Steroids[1]

During the course of some related work, a study was made of the photocondensation of steroids and a mechanism evolved which appears to explain all the known data on this reaction and predicts possibilities for future work.

WINDAUS and BORGEAUD[2] found that ergosterol (I) undergoes dehydrogenation and condensation when exposed to light in the absence of oxygen and in the presence of certain sensitizers (such as fluorescein or cosin). The sensitizer also acts as hydrogen acceptor. The dimer, bisergostadienol (II), (at first erroneously named "ergopinacol") on pyrolysis, produces a new compound, neo-ergosterol (III). From the known structure of neo-ergosterol [1,2]), INHOFFEN[3] deduced a formula for bisergostadienol. His sole basis was SCHMIDT's double bond rule, which states that on pyrolytic rupture a bond once removed from a double bond is preferentially broken. The formula accounts for the scission both at the 7·7′ bond and at the angular C-10 methyl groups.

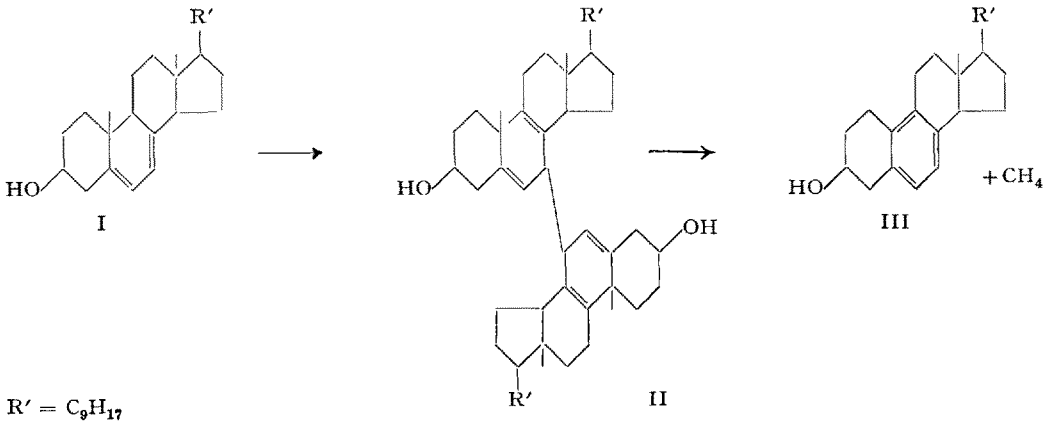
[1] Abstracted from the dissertation which is being submitted to the Faculty of the Graduate School of the Polytechnic Institute of Brooklyn in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

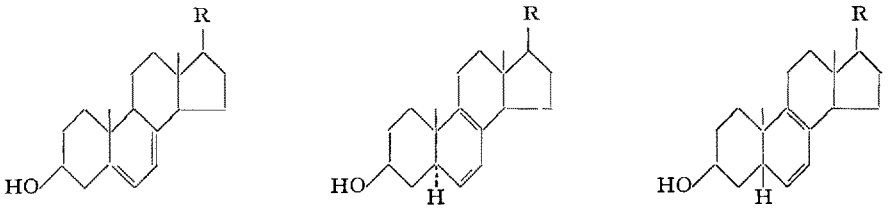
[2] A. WINDAUS and P. BORGEAUD, Ann. Chem. *460*, 235 (1928).

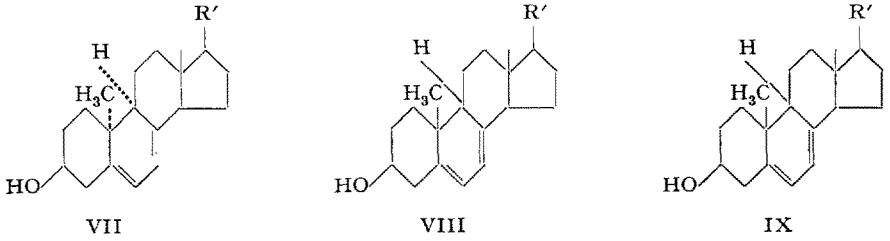
[1] KURT BONSTEDT, Z. Physiol. Chem. *185*, 165 (1929).

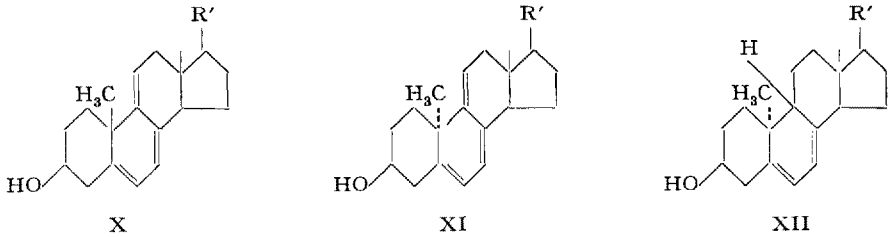
[2] H. HONIGMANN, Ann. Chem. *511*, 292 (1934).

[3] HANS H. INHOFFEN, Naturwissenschaften *25*, 125 (1937).









In 1936 SCHENCK *et al.*[1] in Germany and URISHIBARA and ANDO[2] in Japan found a similar dimerization for 7-dehydrocholesterol (IV), and an analogous pyrolysis product, norsterol. They assumed a structure for the bisteroid parallel to INHOFFEN's formula for the ergosterol dimer.

WINDAUS and ZUHLSDORF[3] obtained the same dimolecular steroid from $\Delta^{6,8}$-cholestadienol (V) and $\Delta^{6,8}$-coprostadienol (VI) as had been isolated from 7-dehydrocholesterol.

TOMINAYA[4] showed that the hydroxyl group at C-3 is superfluous for this photodimerization when he found that irradiation of $\Delta^{5,7}$-cholestadiene led to the formation of a bisteroid.

KENNEDY and SPRING[1] utilized the capacity of several ergosterol isomers to undergo this photochemical reaction as an aid in determining their spatial configuration at C-9 and C-10. The inability of lumisterol (VII) and isopyrocalciferol (VIII), and the ability of ergosterol (IX), dehydroergosterol (X), dehydrolumisterol (XI) and pyrocalciferol (XII) to condense photochemically point to the steric relationship of the methyl at C-10 and the hydrogen at C-9 as the determining factors. These groups were taken to be trans in the isomers that gave dimers (IX and XII) and cis in those that did not (VII and VIII).

Steroids with unsaturation in ring *A* have also been subjected to this reaction. JACOBSEN and NAWROCKI[2] exposed $\Delta^{2,4}$-cholestadiene (XIII) to tungsten light and obtained a dimolecular product, for which a 3,3′ bond was suggested.

[1] FR. SCHENCK, K. BUCHOLZ, and O. WIESE, Ber. Dtsch. Chem. Ges. *69*, 2696 (1936).

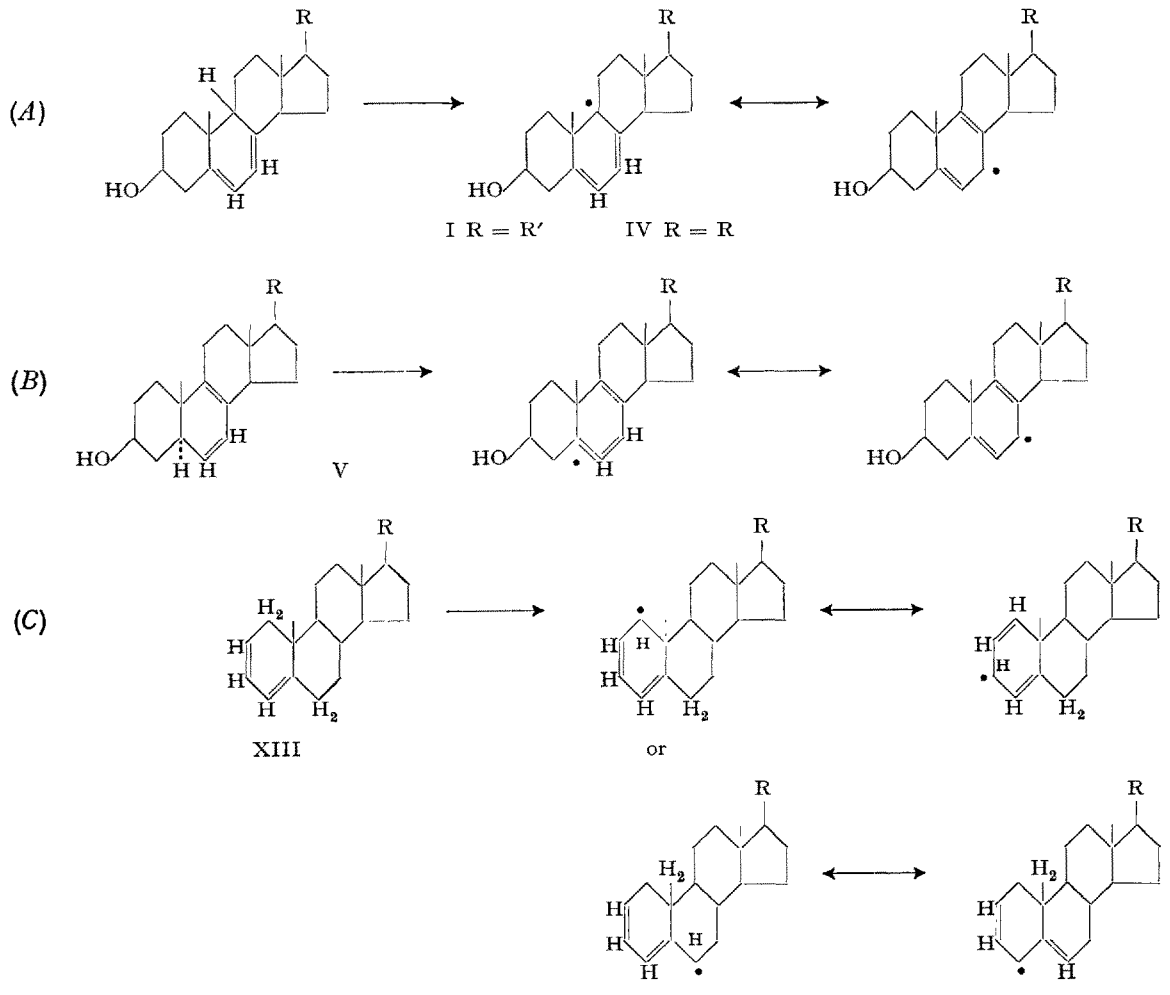
[2] YOSHIYUKI URISHIBARA and TOSHIO ANDO, Bull. Chem. Soc. Jap. *11*, 802 (1936); *12*, 495 (1937) in English. – TOSHIO ANDO, Bull. Chem. Soc. Jap. *14*, 285 (1939); *14*, 482 (1939).

[3] A. WINDAUS and G. ZUHLSDORF, Ann. Chem. *536*, 204 (1938).

[4] AKIRA TOMINAGA, Bull. Chem. Soc. Jap. *14*, 486 (1939).

[1] T. KENNEDY and F. S. SPRING, J. Chem. Soc. 250 (1939).

[2] ROBERT P. JACOBSEN and C. Z. NAWROCKI, J. Amer. Chem. Soc. *62*, 2612 (1940).



The exposure of the same diene to sunlight by USHAKOV and KOSHELEVA[1] led to the formation of a dimer isomeric with JACOBSEN's. The Russian investigators also condensed $\Delta^{3,5}$-cholestadiene (XIV) and obtained the same dimer as from the 2,4 diene.

The work of JACOBSEN and USHAKOV has been repeated and confirmed by the author.

No proposed mechanisms for any of these photocondensations have appeared. The mechanism suggested below accounts for all known dimerizations, including the formation of the same dimer from three steroids (IV, V and VI), and the isolation of two dimers from the same steroid (XIII).

Since all the reactions under discussion proceed under the influence of light (and with the loss of an atom of hydrogen), the assumption is made that a free radical mechanism is operative, with the ejection of the atom of hydrogen—from a carbon in or near the activating diene system—producing the radical.

In ergosterol (I) and 7-dehydrocholesterol (IV) the hydrogen can be lost from the 6, 7 or 9 position. Of these possibilities, only loss of hydrogen from C-9 produces a radical capable of stabilization by resonance (Form. *A*).

This resonance permits the odd electron to be at C-9 or C-7. Since the 9 position is sterically hindered, coupling should proceed best at C-7. This gives a dimer with precisely the formula proposed by INHOFFEN (II).

$\Delta^{6,8}$-cholestadienol (V) can lose hydrogen from the 5, 6 or 7 position, of which only loss from C-5 produces a resonating radical (Formulæ *B*).

Since the 5 position is sterically hindered, coupling should occur at the 7 position. Combination at C-7 will produce the same dimer from the 6,8 diene as from the 5,7 diene, which has been experimentally verified.

Inasmuch as this mechanism requires the elimination from $\Delta^{6,8}$-coprostadienol (VI) of the C-5 hydrogen, its configuration in the monomer does not affect the structure of the dimer. This accounts for the formation of the same bisteroid from this diene, too.

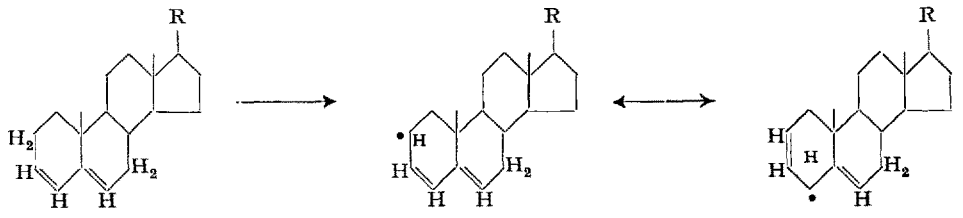
The application of this reasoning to the ergosterol isomers (VII, VIII, IX and XII) studied by KENNEDY and SPRING[1] calls for the removal of the hydrogen atom on C-9. A study of molecular models has shown the C-9 hydrogen to be hindered if the C-10 methyl is cis to it. The expected greater ease of eliminating an unblocked hydrogen atom explains the deduction[1] that ergosterol isomers form photodimers if the C-10 methyl and the C-9 hydrogen are trans.

The fact that two different dimers were obtained[2] from $\Delta^{2,4}$-cholestadiene (XIII) may be resolved by the following argument. This diene can lose a hydrogen atom from the 1, 2, 3, 4 or 6 position, of which only loss from the 1 or 6 position will produce resonance-stabilized radicals (Formulæ *C*).

[1] M. I. USHAKOV and N. F. KOSHELEVA, J. Gen. Chem. U.S.S.R. *11*, 203 (1941).

[1] T. KENNEDY and F. S. SPRING, J. Chem. Soc. 250 (1939).
[2] M. I. USHAKOV and N. F. KOSHELEVA, loc. cit.

(*D*)



XIV

Of the four possible positions for coupling—1,3,4 and 6—none can be eliminated for steric reasons, but two of these—3 and 4—would be favored because they are once removed from two double bonds, whereas the other two possible positions are merely allylic to one double bond. The dimer from $\Delta^{2,4}$-cholestadiene could therefore be either a 3,3′ or a 4,4′ bisteroid.

Since two dimers have actually been found, there remains to be determined, if possible, which bisteroid was isolated by each of the investigators.

Applying the reasoning used previously to the condensation of $\Delta^{3,5}$-cholestadiene (XIV)[1], it is apparent that this diene could couple best at the 4 position (Formulæ *D*).

Considering that the same dimer was obtained by USHAKOV and KOSHELEVA[1] from the 3,5 diene and the 2,4 diene, it follows that their dimer should be the 4,4′ compound, while JACOBSEN and NAWROCKI's dimer[2] should be the 3,3′ compound. This corresponds to the suggestions of these investigators made purely on intuitive reasoning.

JOSEPH L. OWADES[3]

Department of Chemistry, Polytechnic Institute of Brooklyn, January 6, 1950.

Acknowledgments

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Zusammenfassung

Es wird eine Anzahl verwandter Reaktionen der Steroide vergleichend betrachtet. Ein Reaktionsmechanismus wird vorgeschlagen, der sämtliche bekannte Vorgänge zu erklären vermag und der es ermöglicht, die Struktur der entstehenden Bisteroide vorherzusagen.

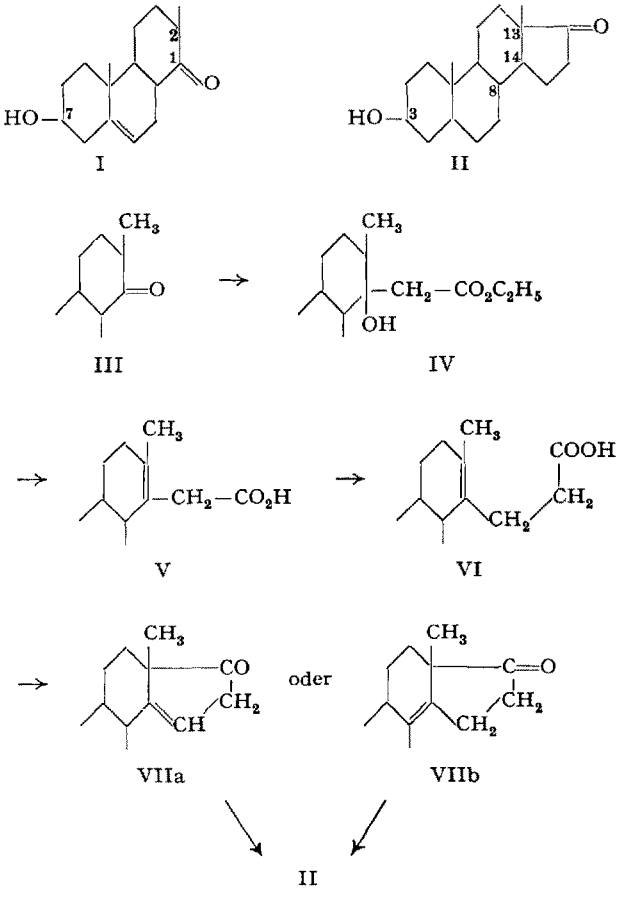
[1] M. I. USHAKOV and U. F. KOSHELEVA, loc. cit.

[2] ROBERT P. JACOBSEN and L. Z. NOVROCKI, loc. cit.

[3] Present address: Fleischmann Laboratories, Standard Brands, Inc., 810 Grand Concourse, New York 51, N.Y.

Darstellung von 4-Ring-Ketonen aus dem trizyklischen Keton von Köster und Logemann[1]

Das trizyklische Keton I von KÖSTER und LOGEMANN[2] entsteht neben Dehydro-3β-androsteron in beachtlichen Mengen bei der Chromsäureoxydation von Cholesterin nach RUZICKA und WETTSTEIN[1]. An anderem Ort[2] berichteten wir ausführlich über eine Reihe seiner Abkömmlinge. Im Zuge der Verwertung der Nebenprodukte der Cholesterinoxydation versuchten wir unter anderem durch Anbau eines 5-Ringes an das trizyklische Keton in die Androsteronreihe (II) zu gelangen. Dies schien um so interessanter, als CORNFORTH und ROBINSON[3] kürzlich die Totalsynthese eines dem trizyklischen Keton nahestehenden Diketons beschrieben.



Für den Anbau des 5-Ringes empfahl sich eine Reaktionsfolge, wie sie durch die Teilformeln III bis VII gekennzeichnet wird. Ein solcher Weg ist in ähnlich gearteten Fällen schon öfters versucht worden[4]. In der

[1] 96. Mitteilung der Reihe «Über Steroide» (95. Mitt. siehe Helv. chim. acta *33*, 388 (1950).

[2] H. KÖSTER und W. LOGEMANN, Ber. Dtsch. chem. Ges. *73*, 298 (1940).

[1] L. RUZICKA und A. WETTSTEIN, Helv. chim. acta *18*, 986 (1935).

[2] Siehe Note 1, Kolonne links.

[3] J. W. CORNFORTH und R. ROBINSON, Nature *160*, 737 (1947); J. Chem. Soc. London, 1855 (1949).

[4] J. W. COOK und C. A. LAWRENCE, J. Chem. Soc. London, 1637 (1935); 817 (1937). – C. K. CHUANG, Y. L. TIEN und C. M. MA, Ber. Dtsch. chem. Ges. *69*, 1494 (1936). – C. D. NENITZESCU, E. CIORANESCU und V. PRZEMETZKY, ib. *73*, 313 (1940).