Tetrahedron Letters No. 20, pp. 909-912, 1962. Pergamon Press Ltd. Printed in Great Britain.

ON THE SELENIUM DEHYDROGENATION OF 3β,12β,20β-TRIHYDROXY-5α-PREGNANE AND A C-NOR-D-HOMOPREGNANE DERIVATIVE[1]

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(Received 2 July 1962)

DURING recent years, a number of polyoxygenated C_{21} aglycones have been isolated from the ester-glycosides which are found in Asclepiadaceae plants.[2] On selenium dehydrogenation, some of these substances afforded the Jacobs hydrocarbon[2b,2e,3] which had been obtained from the Veratrum alkaloids, jervine and veratramine by Jacobs and his colleagues.[4] These dehydrogenation experiments suggested the possibility that the C_{21} aglycones belong to the C-nor-D-homopregnane series and tentative formulas having the C-nor-D-homo skeleton were assigned to some of them.[5] There also exists the possibility that the normal steroids could give the Jacobs hydrocarbon on dehydrogenation. To clarify this question, we attempted the selenium dehydrogenation of a 12β substituted pregnane derivative and C-nor-D-homo-pregnane derivative.[6]

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[1] For convenience, by the term, C-nor-D-homopregnane, we mean the compound which biogenetically corresponds to the normal pregnane and should be called 17α-methyl-D-homo-12,18-bisnorpregnane by the IUPAC system.

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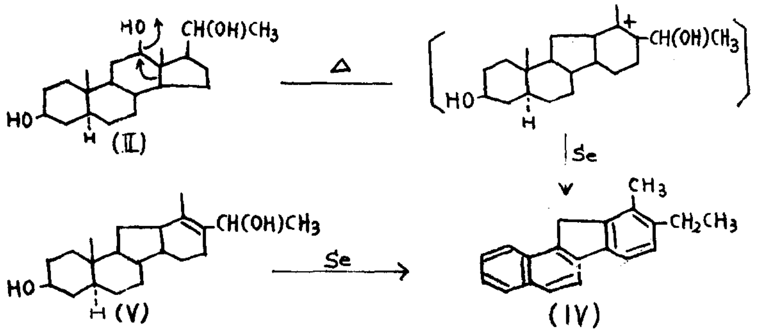
[3] a H. Mitsuhashi and Y. Shimizu, Chem. Pharm. Bull. 7, 749 (1959); 8, 738 (1960); b J.M. Nascimento, H. Jaeger, Ch. Tamm and T. Reichstein, Helv. Chim. Acta 42, 661 (1959).

[4] W.A. Jacobs, C.C. Craig and G. LaVin, J. Biol. Chem. 141, 51 (1941); W.A. Jacobs and Y. Sato, Ibid. 181, 55 (1949).

[5] H. Mitsuhashi and Y. Shimizu, Chem. Pharm. Bull. 7, 949 (1960); 9, 433 (1962). J.W. Cornforth, Chem. & Ind. (London), 602 (1959).

[6] In this respect, Reichstein and his colleagues also studied the dehydrogenation of uscharidin and Δ^5-pregnene-3,20-diol. M.S. Bharacha, G. Hesse, Herb. Jäger, Ek. Weiss and T. Reichstein, Helv. Chim. Acta 45, 93 (1962); M.S. Bharacha, Ek. Weiss and T. Reichstein, Ibid. 45, 103 (1962).



3β,12β,20β-Trihydroxy-5α-pregnane (II) (m.p. 256°, 2.4 g), which was prepared by the NaBH$_4$ reduction of 3β,20β-dihydroxy-5α-pregn-12-one (I),[7] was dehydrogenated with twice the amount of selenium under a nitrogen atmosphere at ca. 310° for 24 hr. The n-hexane soluble part of the ether extract, which was a crystalline solid, was separated by chromatography into two crystalline fractions, (A) 290 mg and (B) 458 mg. (A) was recrystallized from acetone-MeOH to fine plates (III), m.p. 95-99°, 70 mg. (B) gave plates (IV), m.p. 148-152°, 220 mg, which proved to be a very pure sample of the Jacobs hydrocarbon by I.R. and U.V. spectra. The mixed melting point with the synthetic material[8] also confirmed the identity.[9]

The I.R. absorption indicates that III has no hydroxyl nor carbonyl group and seems to be an unknown hydrocarbon (Fig. 1). The U.V. absorption maximum is at much a longer wavelength (272 mμ) suggesting the presence of a highly conjugated system (Fig. 2). It would be surprising if the main dehydrogenation product were the Jacobs hydrocarbon and the cyclopentenophenanthrene product could not be found in the products. In the dehydrogenation procedure, the pyrolytic removal of 12β-hydroxy group caused the C-nor-D-homoannulation[10] prior to dehydrogenation.

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[7] D.N. Kirk, D.K. Patel and V. Petrow, J. Chem. Soc. 1046 (1957).

[8] L. Keller, Ch. Tamm and T. Reichstein, Helv. Chim. Acta 41, 1633 (1958).

[9] The melting point was kindly measured by Prof. T. Reichstein.

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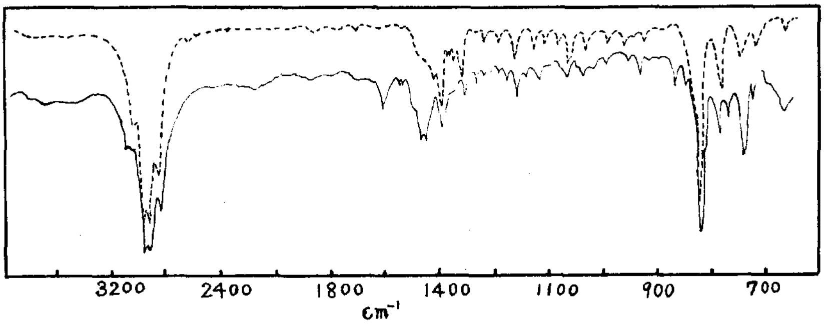

FIG. 1

Infra-red spectra of III (in CS_2) and VI (in KBr).

----(III), ——(VI)

For the comparison, compound (V), which surely has the C-nor-D-homo-pregnane skeleton,[11] (1.2 g) was dehydrogenated as in the case of (II). The n-hexane soluble crystalline solid was separated into two crystalline parts, (C) 28 mg and (D) 160 mg. Recrystallization of (C) and (D) easily gave pure crystals (VI) 9 mg and (IV') respectively.

FIG. 2

Ultra-violet spectra of III and VI (in cyclohexane).

----(III), ——(VI)

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[11] The synthesis and confirmation of this compound was reported at 14th Annual Meeting of Pharmaceutical Society of Japan, Sapporo, and will soon be published.

IV', m.p. 148-152°, was identified with the Jacobs hydrocarbon by the spectral data and the mixed melting point. VI, m.p. 93°, is an unknown substance and its absorption spectra (Figs. 1 and 2) are clearly different from those of III.

From the above experiment, it can be reasonably concluded that the production of the Jacobs hydrocarbon in the selenium dehydrogenation does not necessarily mean the presence of the C-nor-D-homo ring system.

Acknowledgement - We wish to express our thanks to Prof. T. Reichstein, Basel, for his kind co-operation in the identification of the Jacobs hydrocarbon.