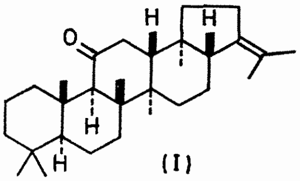
Synthesis of 18α-Fernane Derivatives. A Backbone Rearrangement of Pentacyclic Triterpenes

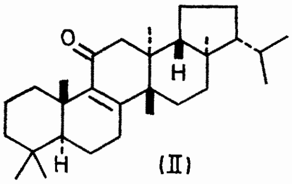
By HIROSHI KAKISAWA* and KAZUO IGUCHI

(*Department of Chemistry, Tokyo Kyoiku University, Otsuka, Tokyo, Japan*)

Summary Acid-catalysed deacetylation and rearrangement of an 11-oxo-γ-onocerin derivative are accompanied by inversion of the configuration at C-18, giving a conjugated ketone, the structure of which is proved by converting it into hopene-II.

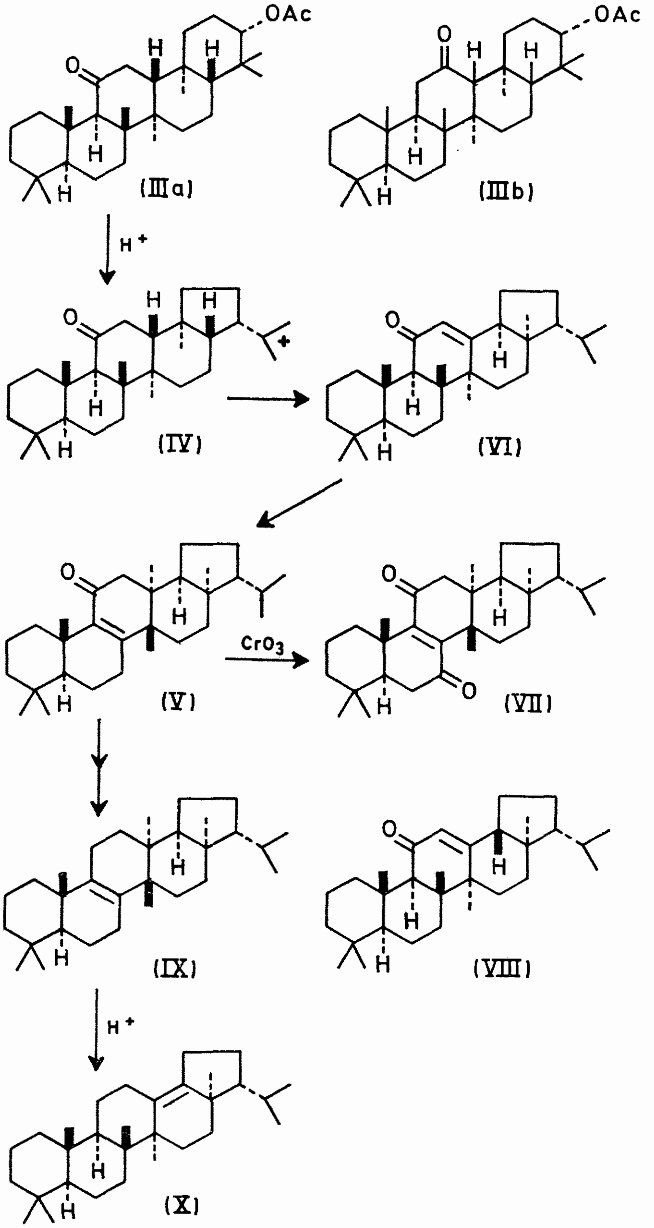
WE have reported[1] the synthesis of fern-8-ene from ferna-7,9(11)-diene, which was prepared from hopa-9(11), 21-diene by acid-catalysed migration of one double bond from position 21 to position 7, conjugated with the 9(11)-double bond. If this type of reaction also occurred in hop-21-en-11-one (I) to afford an αβ-unsaturated ketone (II) by migration of the double bond to position 8, conjugated with the carbonyl group, and if the reaction proceeded in a single concerted process, the resulting product (II) could be an intermediate for the synthesis of fern-9(11)-ene. We report that the acid-catalysed rearrangement of keto-acetate (IIIa) affords an αβ-unsaturated ketone (V) having an α-hydrogen atom at C-18.


(I)


(II)

Hydriodic acid treatment of a mixture consisting of equal amounts of keto-acetates (IIIa) and (IIIb), prepared from a mixture of 21-deoxy-acetyl-γ-onocerin and 3-deoxy-acetyl-γ-onocerin[1] by oxidation with hydrogen peroxide in acetic acid,[2] afforded the αβ-unsaturated ketone (V) in 25% yield, together with another αβ-unsaturated ketone (VI, 6%) and an ill-defined oily substance. The main product (V) had m.p. 214—215°; ν_{max} (KBr) 1645, 1590 cm^{-1}; λ_{max} (EtOH) 259 nm (ε 8100), and the enone (VI) had m.p. 161—164°; ν_{max} (KBr) 1665 cm^{-1}; λ_{max} (EtOH) 248 nm (ε 11,000). These properties indicate that the main product has the gross structure (V), and this structure was confirmed by oxidation of (V) with chromic acid to afford an enedione (VII), m.p. 166—167°, having the characteristic spectral properties of a transoid enedione: ν_{max} (KBr) 1680 and 1670 cm^{-1}; λ_{max} (EtOH) 272 nm (ε 6100). Although the mass spectrum of the unsaturated ketone (V) was very similar to that of authentic fern-8-en-11-one (II), the i.r. spectra of the two compounds were clearly different. Thus the new αβ-unsaturated ketone obtained from keto-acetate (IIIa) was expected to be a stereoisomer of fern-8-en-11-one (II). These results show that the series of hydride and methyl migrations in the reaction from carbonium ion (IV) to αβ-unsaturated ketone (V) is not a one-step process, but proceeds through an intermediate such as (VIII), which isomerizes to a stereoisomer (VI), the C-18 epimer of (VIII).

This explanation was rationalized by the conversion of the enone (V) into a known compound, hopene-II (X), in which C-18 is trigonal. Reduction of the αβ-unsaturated ketone (V) with lithium aluminium hydride afforded an allylic alcohol which, upon acid treatment, gave a heteroannular 7,9(11)-diene, m.p. 156°, λ_{max} (EtOH) 233 (ε 12,500), 240 (13,600), and 248 nm (8600). Birch reduction of the diene with lithium–ethylamine afforded a mono-ene (IX), m.p. 144—148°, which was treated with sulphuric acid in acetic acid to give an isomeric mono-ene. The



resultant mono-ene was identical with authentic hopene-II (X) in all respects (i.r. and mass spectra, t.l.c., m.p., and mixed m.p.). Thus the $\alpha\beta$-unsaturated ketone obtained from keto-acetate (IIIa) by acid treatment was 18α-fern-8-en-11-one (V). This is in contrast with Spring's observation[3] that 3-acetoxyolean-11-one was converted on acid treatment into an $\alpha\beta$-unsaturated ketone with retention of the configurations about the *trans*-hydrindane ring junction.

We thank Professor H. Ageta of Showa College of Pharmacy for valuable discussions and gifts of fernane derivatives.

(*Received, September 2nd,* 1970; *Com.* 1461.)

---

[1] K. Iguchi and H. Kakisawa, preceding communication.

[2] D. H. R. Barton and K. H. Overton, *J. Chem. Soc.*, 1955, 2639.

[3] G. G. Alan, M. B. E. Fayez, F. S. Spring, and R. Stevenson, *J. Chem. Soc.*, 1955, 3378.