[Chem. Pharm. Bull. 13(5) 631~632 (1965)]

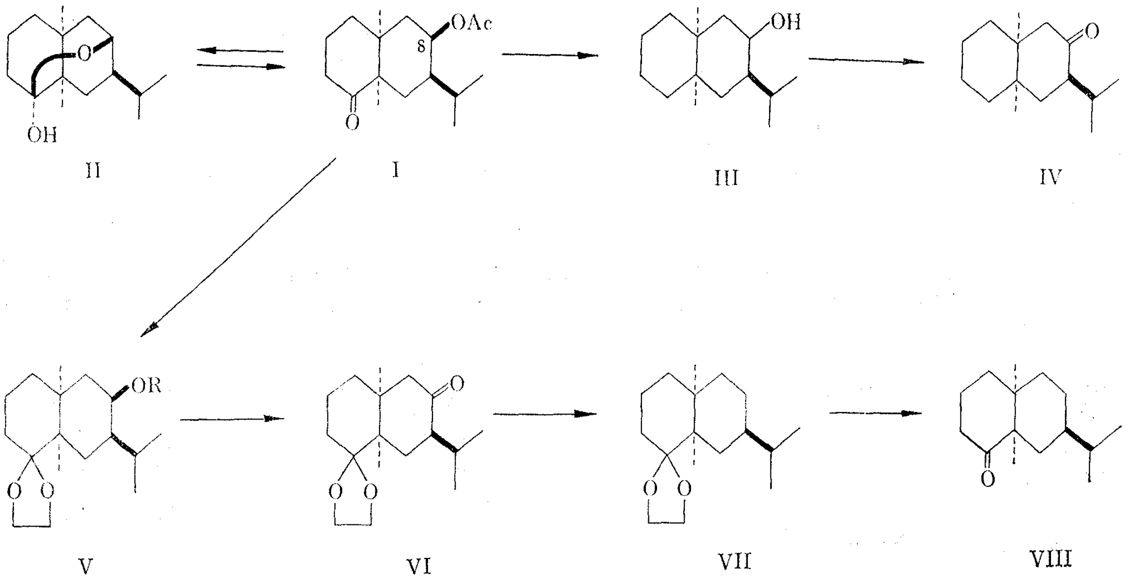
UDC 581.19 : 547.597 : 582.975

Structure of Fauronyl Acetate and Cryptofauronol

The new sesquiterpenoids, fauronyl acetate and cryptofauronol, have recently been isolated from a wild Japanese valerian.[1] The present communication provides evidence for the structure and absolute configuration of fauronyl acetate and cryptofauronol, as indicated in formulas (I) and (II), respectively, and for their conformation.

Fauronyl acetate (I), $C_{17}H_{28}O_3$, mol. wt. 280 (mass spec.), m.p. 85~86°, $[\alpha]_D$ −77.6°,[*1] is a saturated bicyclic ketol acetate as revealed by the spectroscopic data: *e.g.*, the infrared spectrum shows bands at 1695 (cyclohexanone), 1733, and 1234 cm^{-1} (acetoxyl), and the nuclear magnetic resonance spectrum exhibits a 3H singlet at 7.99 τ ($C\underline{H}_3$-CO-O-) and a 1H doublet (broad) at 4.90 τ ($\underline{H}$-C$\leqslant$O-Ac); both show no sign of unsaturation. The acetate (I) was characterized as the semicarbazone, $C_{18}H_{31}O_3N_3$, m.p. 218.5~220°.

Alkaline hydrolysis of fauronyl acetate (I) was found to give cryptofauronol (II), $C_{15}H_{26}O_2$, m.p. 90~91°, $[\alpha]_D$ −7.4°, whose hemiketal nature was confirmed by the facts which follow. 1) The infrared spectrum shows a band at 3390 cm^{-1} (hydroxyl) but lacks a band attributable to a carbonyl group. 2) The nuclear magnetic resonance spectrum discloses a 1H doublet (broad) at 6.08 τ ($\underline{H}$-C$\leqslant$O-). 3) On refluxing with acetic anhydride in the presence of sodium acetate fauronyl acetate (I) was regenerated.



Wolff-Kishner reduction of fauronyl acetate (I) or its semicarbazone formed the mixture of alcohols (III), which on chromic acid oxidation gave the ketone (IV), $C_{15}H_{26}O$, mol. wt. 222 (mass spec.), n_D^{25} 1.487, $[\alpha]_D$ +59.9°, infrared band (liquid) at 1715 cm^{-1} (cyclohexanone). The position of the carbonyl group between a methylene and a methine group in the ketone (IV) was established by the observations described below. 1) The infrared spectrum shows a band at 1424 cm^{-1} (methylene α to carbonyl). 2) The nuclear magnetic resonance spectrum exhibits a 2H AB quadruplet at 7.60 and 8.24 τ (J=14.0,

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[*1] Analytical values are in agreement with the molecular formulas shown. $[\alpha]_D$s refer to $CHCl_3$ solution and IR spectra to KBr disk unless otherwise stated. NMR spectra were measured at 60 Mc. in CCl_4 solution *vs.* $(CH_3)_4Si$ as internal reference. Chemical shifts are given in τ-values and coupling constants (J) in c.p.s.

[1] H. Hikino, Y. Hikino, Y. Takeshita, H. Kato, T. Takemoto: Yakugaku Zasshi, 85, 179 (1965).

$\geqslant$C–C$\underline{H}_2$–CO–). 3) Base-catalyzed deuteration converted it into the trideuterio-derivative, mol. wt. 225 (mass spec.), infrared bands (liquid) at 1715 (cyclohexanone), 2212, 2112 cm^{-1} (C–D), no active methylene band.

The skeleton, including the position of the carbonyl group of fauronyl acetate, was proved in the following way. Fauronyl acetate (I) was converted into the ketal-acetate (V; R=Ac), $C_{19}H_{32}O_4$, m.p. 114~115°, $[\alpha]_D$ −27.7°, infrared bands at 1733, 1239 (acetoxyl), 1195, 1075 cm^{-1} (ketal), which on alkaline hydrolysis gave the ketal-alcohol (V; R=H), $C_{17}H_{30}O_3$, m.p. 85.5~86.5°, $[\alpha]_D$ +31.3°, infrared bands at 3401 (hydroxyl), 1195, 1082 cm^{-1} (ketal). Oxidation of the alcohol (V; R=H) with chromium trioxide–pyridine complex to the ketone (VI), infrared bands (liquid) at 1712 (cyclohexanone), 1195, 1080 cm^{-1} (ketal), and subsequent Wolff–Kishner reduction gave the ketal, $C_{17}H_{30}O_2$, n_D^{25} 1.489, $[\alpha]_D$ +12.7°, infrared bands (liquid) at 1198, 1078 cm^{-1} (ketal), identified as valeranone ketal(VII).[2] This, when hydrolysed with acid, furnished the ketone, $C_{15}H_{26}O$, n_D^{25} 1.490, $[\alpha]_D$ −40.9°, infrared band (liquid) at 1702 cm^{-1} (cyclohexanone), whose properties are identical with those of valeranone (VIII)[3].

The combined evidence establishes that fauronyl acetate and cryptofauronol are represented by stereoformulas (I) and (II), respectively.

The optical rotatory dispersion curve of fauronyl acetate giving a negative Cotton effect (a, −154) is almost superimposable upon those of valeranone (a, −141), kanokonol (a, −149), and kanokonyl acetate (a, −124).[2,4] This, together with the observation that the C-8 hydrrogen signal shows it to be equatorial, indicates that fauronyl acetate has an all-chair conformation with the isopropyl group equatorial. Therefore, the transformation from fauronyl acetate to cryptofauronol, a compound having a rigid conformation, must involve ring conversion of the decalin system with concomitant deformation into a boat form of the isopropyl bearing ring.

On hydrolysis of fauronyl acetate (I) the formation of the hemiketal, cryptofauronol (II), provides unambiguous chemical evidence of a *cis* ring junction of the valerane skeleton.

The authors wish to express their sincere thanks to Research Laboratories, Takeda Chemical Industries, Ltd., for the NMR spectra and to Research Laboratory, Shionogi & Co., Ltd., for the ORD curve.

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Received February 18, 1965

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[4] H. Hikino, Y. Takeshita, Y. Hikino, T. Takemoto: *Ibid.*, **13**, 626 (1965).