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THE CONSTITUENTS OF PETASITES JAPONICUS MAXIM. RHIZOMES

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In the present paper we report the isolation and structural determination of the components from the rhizomes of Petasites japonicus Maxim. (Japanese name "Fuki"). Recently Herout, Šorm and their colleagues have investigated extensively the constituents of the rhizomes of Petasites species, and found many members of eremophilane type furanosesquiterpenes. We have isolated fifteen components, which included four known and six unknown furoeremophilanes. The ethereal extract from the dried rhizomes of the plant was subjected to steam-distillation or column chromatography on deactivated neutral alumina (Merck, grade III). The known 3-carene, eremophilene,[1] α-santalene, thymol methyl ether, furanoeremophilane,[1] ligularone (XI),[2] petasalbin angelate (albopetasin),[3,4] petasalbin (VIII),[2] 6-hydroxyeremophilenolide[4] and six new furan derivatives were obtained by GLC and repeated column chromatography. They were named petasalbin methyl ether (I), furanofukinol (II), 6-acetylfuranofukinol (III), 6-angelylfuranofukinol (IV), S-furanopetasitin (V) and furanojaponin (VI) respectively. All these components I-VI were positive to Ehrlich's furan test and then proved to be eremophilane derivatives by the following study.

Petasalbin methyl ether (I), $C_{16}H_{24}O_2$, b.p. 90-100° (bath temp)/4×10^{-4}mmHg; $[\alpha]_D$ -52.5°; m/e 248 M^+; IR: 1638,1565 cm^{-1} (furan); λ_{max}^{EtOH} 219.5 mμ; δ^{CDCl_3}: 7.0 (q, J=1 Hz), 2.03 (d, J=1 Hz) due to a grouping O-CH=C-Me on a furan ring, 6.08 (s, C-6 H), 3.35 (s, OMe), 1.05 (s, C-Me), 0.75 (br d, J=6 Hz, CH-Me); m/e 138 due to a fragment (VII)[5] characteristic of a furan ring containing a MeO group at the allylic position. The above data lead to the tentative formula (I). This conclusion was confirmed by the synthesis of I which was accomplished by methylation of the known petasalbin VIII with t-BuOK-MeI.

All the other compounds II-VI also showed almost similar spectra (UV, IR and

NMR) assignable to a furan ring as those of I described above. In addition, each alkaline hydrolysis of compounds III, IV and V yielded the same neutral product, which was identical with the natural furanofukinol II, and its acidic part respectively.

Furanofukinol (II), $C_{15}H_{22}O_3$, m.p. 178-180° (dec); IR: 3367 cm^{-1} (OH). Oxidation of II with CrO_3-pyridine yielded a diketone (IX), $C_{15}H_{18}O_3$, m.p. 149-150°, IR: 1700 (sat. 6-membered ring ketone), 1660 cm^{-1} (α,β-unsat. ketone); λ_{max}^{EtOH} 269 mμ characteristic of a furan conjugated with C-6 keto-group.[6] The diketone was converted to a monothioketal (X) and followed by desulfurization to afford the known ligularone (XI).[2] On the other hand, the IV-tosylate was reduced with LAH to yield the known petasalbin VIII. The stereochemistry of VIII has been established by Novotný et al.[2,7] Hence the one OH group in II was ascertained to be a 6β-OH. The location and configuration of the other OH group were established as follows. The diketone IX had a sat. 6-membered ring ketone (IR: 1700 cm^{-1}) and showed δ^{CDCl_3}: 2.8 (q, J=6.5 Hz) assignable to a C-4 H coupled with a C-14 Me at 0.80 (d, J=6.5 Hz). This feature suggests a keto-group at C-3. The controlled oxidation of II with CrO_3-pyridine gave a ketol (XII); IR: 3410 (OH), 1665 cm^{-1} (α,β-unsat. ketone); λ_{max}^{EtOH} 269 mμ indicating the presence of C-6 keto-group. Dehydration of XII with $POCl_3$-pyridine afforded a product (XIII), m.p. 66-67° which showed δ^{CDCl_3}: 1.73 (d, J=1.2 Hz) and 5.43 (m) due to C-14 Me and C-3 H respectively. The above results led to the formula (XIII) for the dehydration product. In the NMR spectra of II and its derivatives (III and IV), the half-band widths of C-3 protons closely similar to that of C-3 H of isopetasin (XIV)[8] were ca. 14 Hz indicating the axial nature. Consequently, the structure of furanofukinol can be assigned as in stereoformula II.

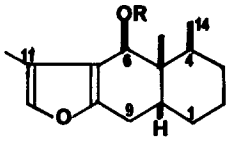
6-Acetylfuranofukinol (III), a viscous oil, showed IR: 3320 (OH), 1710 and 1240 cm^{-1} (acetate); δ^{CDCl_3}: 2.18 (s) and 6.34 (s) for a grouping CH-OAc. Acetylation of III with Ac_2O-pyridine yielded a diacetate, m.p. 144-145° which was identical with furanofukinol diacetate (XV). It must be represented by the formula III.

6-Angelylfuranofukinol (IV), $C_{20}H_{28}O_4$, a viscous oil, showed the following spectral data; IR: 3440 (OH), 1700 and 1230 cm^{-1} (α,β-unsat. ester); δ^{CDCl_3}: 6.50

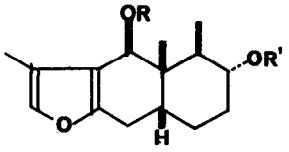
(s, C-6 H), 4.40 (m, C-3 H), 2.70 (s, OH). Oxidation of IV with CrO_3-pyridine gave a monoketone (XVI) whose UV spectrum showed λ_{max}^{EtOH} 218 mμ as similar to that of IV and IR: 1705 cm^{-1}, indicating the presence of a sat. ketone. The results of the alkaline hydrolysis of IV and the reductive transformation of the IV-tosylate to VIII lead to the formula IV for this compound.

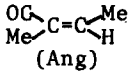
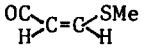
S-Furanopetasitin (V), $C_{24}H_{32}O_5S$, m.p. 107-108°, $[\alpha]_D$ -60.5°, had two unsat. ester groups; IR: 1713, 1699, 1230, 1214 cm^{-1}; λ_{max}^{EtOH} 216 and 287.5 mμ; δ^{CCl_4}: 1.96 (s, 3H), 2.03 (d, J=8 Hz, 3H), 6.12 (q, J=8 Hz, 1H) due to the angelyl group ;[9] 2.38 (s, -S-Me), 5.82 (d, 1H) and 7.03 (d, 1H) coupled each other with J=11 Hz, due to cis-β-methylthioacrylic ester group. In accordance with the above assignment, alkaline hydrolysis of V with 2N alc KOH furnished cis-β-methylthioacrylic acid and 6-angelylfuranofukinol IV, which was then hydrolyzed with DMSO-t-BuOK to afford furanofukinol II. Thus the structure of S-furanopetasitin is represented as in formula V.

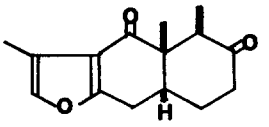
Furanojaponin (VI), $C_{20}H_{28}O_3$, b.p. 110-130° (bath temp)/5×10^{-4}mmHg; m/e 316 M^+, IR: 1708, 1230, 1148 cm^{-1} (α,β-unsat. ester); δ^{CCl_4}: 1.89 (s), 1.96 (d, J=7 Hz), 5.94 (q, J=7 Hz, 1H) due to an angelyl group, 5.05 (m, C-2 H, $W_{1/2}$=ca. 15 Hz). Alkaline hydrolysis of VI gave readily an alcohol which was oxidized with CrO_3-pyridine to yield a ketone (XVII). The ketone showed an IR bands at 1707 cm^{-1} (sat. 6-membered ring ketone). Therefore, the OH group must be located at C-1, C-2 or C-3. The NMR spectrum of the ketone XVII did not show the characteristic signal of the C-4 H caused by the adjacent C-3 C=O group as described before. The remaining position, C-1 or C-2 was examined by deuteration of the ketone XVII with MeOD-MeONa. The comparison of both MS spectra between the original and deuterated ketones indicated the incorporation of four D atoms (m/e 236 M^+) and the same base peak, m/e 147 assignable to a fragment (XVIII). The OH group was, therefore, located at C-2, and its β-(eq)-orientation was indicated by the half-band width (ca. 15 Hz) of the C-2 H signal in the NMR of VI and by the ease of the alkaline hydrolysis of furanojaponin. Then, the structure of furanojaponin can be represented as in formula VI.



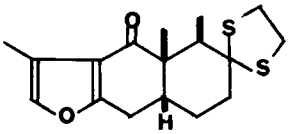
I: R=Me
VIII: R=H



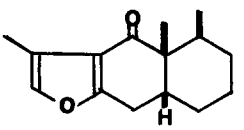
	R=	R'=
II:	H	H
III:	Ac	H
IV:	 (Ang)	H
V:	Ang	
XV:	Ac	Ac



IX



X



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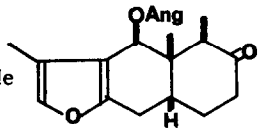
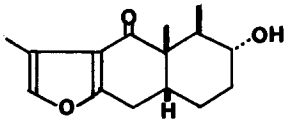


XVI



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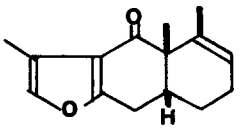

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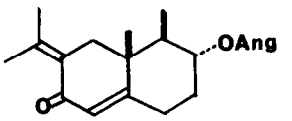
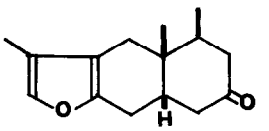
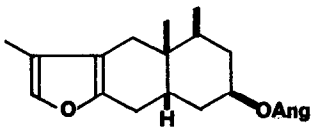


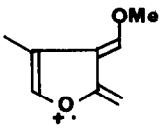
XIV



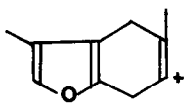
XVII



VI



VII: m/e 138



XVIII: m/e 147

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