Tetrahedron Letters No. 20, pp. 697-701, 1961. Pergamon Press Ltd. Printed in Great Britain.

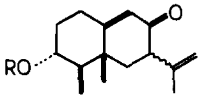
SUBSTANCES FROM *PETASITES OFFICINALIS* MOENCH. AND *PETASITES ALBUS* (L.) GAERTN.

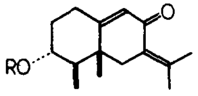
L. Novotný, V. Herout and F. Šorm

Institute of Organic Chemistry and Biochemistry,
Czechoslovak Academy of Science, Prague

(Received 30 October 1961)

DURING recent years, Stoll and co-workers[1] and Aebi, Büchi and Waaler[2-5] investigated substances from coltsfoot rhizomes mainly in connection with their studies concerning spasmolytically active compounds. They isolated new types of substances as e.g. petasin (I), isopetasin (II) and S-petasin (III). The constitution of these interesting substances which are further representatives of sesquiterpenic compounds belonging to eremophilane type, has been elucidated by the authors named at last.[2-5]





I R = $\mathrm{CO\underset{CH_3}{C}=CHCH_3}$ II R = $\mathrm{CO\underset{CH_3}{C}=CHCH_3}$

III R = $\mathrm{COCH=CHSCH_3}$

---

[1] A. Stoll, R. Morf. A. Rheiner and J. Renz, *Experimentia* **12**, 360 (1956). *cf.* also: A. Stoll, J. Renz and R. Morf, *Referatenband XIV. Internationaler Kongress für reine und angewandte Chemie Referat 306*. Zürich (1955).

[2] A. Aebi, J. Büchi, T. Waaler, E. Eichenberger and J. Smutz, *Pharm.* Acta Helv. 30, 277 (1955).

[3] A. Aebi, T. Waaler and J. Büchi, *Pharm. Weekblad* **93**, 397 (1958).

[4] T. Waaler, *Dissertation*, ETH Zurich (Prom. Nr. 2658) Juris Verlag (1958).

[5] A. Aebi and T. Waaler, *Über die Inhaltstoffe von Petasites hybridus (L.) Fl. West.* Verlag Helbing und Lichtenbahn, Basel (1959).

The absolute configuration of petasin has been ascertained by Aebi and Djerassi[6] on the basis of rotatory dispersion measurements and by Herbst and Djerassi[7] on the basis of proofs provided by synthesis. The configuration on carbon atom substituted with isopropylene group remained, however, uncertain.

As a part of an extensive study of sesquiterpenic lactones from Compositae, we had been concerned, at the time the papers mentioned were published, in isolation and structure of compounds from Petasites officinalis Moench., syn. P. hybridus (L.) Fl. Weet. and further from Petasites albus (L.) Gaertn. Chromatography of rhizomes extracts and subsequent crystallisation of particular eluates afforded a series of new compounds, different from those hitherto reported.[1-5] This Communication summarizes our results; it is hoped to publish this work in full detail in a series of papers in Coll. Czech. Chem. Comm.

The substances isolated, the physical constants of which are outlined in Table 1, fall essentially into two parts: substances of furane type [furanoeremophilane (IV), furanoeremophilone (V), petasalbin (VI), albopetasin (VII), albopetasol (VIII) and furanopetasin (IX)] and compounds containing α,β-unsaturated δ-lactonic grouping [eremophylenolide (X), petasitolide A (XI), petasitolid B (XII) and S-petasitolide A (XIII) and B (XIV)]. In both plants, we succeeded to find also the sesquiterpenic hydrocarbon eremophilen (XV) which contains one methylene double bond and one trisubstituted ethylenic linkage. Tentative formulae suggested for compounds IV-VII and IX-XIV may be seen in Fig. 1.

The structures were elucidated especially on the basis of conversion of all mentioned oxygen-containing compounds into the same 8,12-oxidoeremo-

---

[6] A. Aebi and C. Djerassi, Helv. Chim. Acta 42, 1785 (1959).

[7] D. Herbst and C. Djerassi, J. Amer. Chem. Soc. 82, 4337 (1960).

philane (XVI). On hydrogenation and on hydrogenolysis, some compounds (eremophilene, furanoeremophilane, eremophilenolide and petasalbin) afforded even the hydrocarbon eremophilane (XVII) which for comparison purposes was prepared from hydroxydihydroeremophilone.*

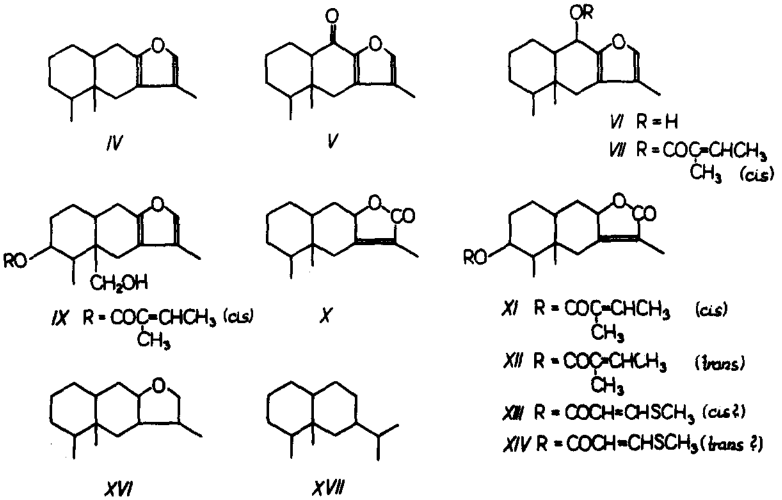


FIG. 1.

The structure of furanoeremophilane (IV; from P. albus) formulae see (Fig. 1) which besides double bonds in the furane ring contains no other ethylenic linkage, followed from the identification of its hydrogenation product. Furanoeremophilone (V; from P. officinalis) has its ketonic carbonyl conjugated with furane ring and its structure ensued from conversion into a derivative, identical with a product of petasalbin reduction. Petasalbin (VI; from P. albus) contains, besides a furane ring, a secondary hydroxyl group in allylic position and structure VI has been allotted to it. Albopetasin (VII; from P. albus) is an angelate ester of petasalbin. Albopetasol (VIII; from P. albus) contains a furane ring and two hydroxyl groups, the location of which is still uncertain. Furanopetasin (IX; from P. officinalis) contains a primary and a secondary hydroxyl group, the latter

---

* We are greatly indebted to Dr. M.D. Sutherland, University of Brisbane, Australia, for a sample of hydroxydihydroeremophilone.

Table 1

Compound	Formula	m.p.	$[\alpha]_D^{20}$	Characteristic bands in the spectrum	
				Infra-red (cm^{-1})	Ultra-violet
Furanoeremophilane IV	$C_{15}H_{22}O$	*	-8.4°	1576,1660, 1776,1810	222 mμ; log ε 3,779
Furanoeremophilone V	$C_{15}H_{20}O_2$	150°	$\pm 0^{\circ}$	1537 3000, 1667	280 mμ; log ε 4,18
Petasalbin VI	$C_{15}H_{22}O_2$	$81-82^{\circ}$	-11.2°	1567,3485 3615	220 mμ; log ε 3,836
Albopetasin VII	$C_{20}H_{28}O_3$	$106-7^{\circ}$	$\pm 0^{\circ}$	1572,1653, 1718	224 mμ; log ε 4,075
Albopetasol VIII	$C_{15}H_{22}O_3$	$178-80^{\circ}$	-24.1°	1568,1652, 3320,3370	220 mμ; log ε 3,817
Furanopetasin IX	$C_{20}H_{28}O_4$	$105-6^{\circ}$	$\pm 0^{\circ}$	1567,1655,1718, 3450,3608	222 mμ; log ε 4,17
Eremophilenolide X	$C_{15}H_{22}O_2$	125°	$+16.6^{\circ}$	1750,1760, 1699,1038	220-224 mμ; log ε 4,162
Petasitolide A XI	$C_{20}H_{28}O_4$	147°	$+48^{\circ}$	1762,1712 1650	218 mμ; log ε 4,420
Petasitolide B XII	$C_{20}H_{28}O_4$	146°	$+31.8^{\circ}$	1761,1713 1650	219 mμ; log ε 4,447
S-petasitolide A XIII	$C_{19}H_{26}O_4S$	$201-2^{\circ}$	-15.3°	1695,1572, 1750	219 mμ; log ε 4,339 288 mμ; log ε 4,223
S-petasitolide B XIV	$C_{19}H_{26}O_4S$	$199-200^{\circ}$	-32.9°	1695,1571, 1750	219 mμ; log ε 4,193 289 mμ; log ε 4,167
Eremophilene XV	$C_{15}H_{24}$	**	-104.2°	885,1642, 1780,3085	

* B.p. $148^{\circ}/16$ mm, d_4^{20} 1,0270; n_D^{20} 1,5172.

** B.p. $132^{\circ}/19$ mm, d_4^{20} 0.9325; n_4^{20} 1,5067.

being esterified with angelic acid. The location of both hydroxyl groups follows, in sense of formula IX, from chemical and physical properties of the substance.[8]

Besides santanolides, alantanolides, guaianolides, the group of newly isolated eremophilenolides represents a further type of sesquiterpenic lactones from Compositae.

Eremophilenolide (X; from P. officinalis) which has the less complicated structure, was converted into eremphilone (XVIII, Fig. 1) by the method used earlier for conversion of santanolide "c" into dihydrojunenol;[9] the infra-red spectrum of XVIII exhibited band at 1430 cm^{-1} due to a methylene group adjacent to ketonic carbonyl (1711 cm^{-1}).

The group of petasitolides and S-petasitolides (XI-XIV); (from P. officinalis) is derived from hydroxyeremophilenolide XIX which is esterified with angelic acid (petasitolide A XI), tiglic acid (petasitolide B XII) and cis- or trans-β-methylthioacrylic acid (S-petasitolide A (XIII) or B (XIV).

---

[8] L. Novotný, Ch. Wlotzka, V. Herout and F. Šorm, Coll. Czech. Chem. Comm. In press.

[9] B.C. Bhattacharyya, A.S. Rao and A.M. Shaligram, Chem. & Ind. 469 (1960).