# A SESQUITERPENIC ALKALOID, EREMOPHILENE LACTAM, FEOM THE RHIZOMES OF *Petasites hybridus**

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From the rhizomes of *Petasites hybridus* (L.) GAERTN., MAYER *et* SCHERB. a substance was isolated of the composition $C_{15}H_{23}NO$. It was shown that this is the first alkaloid of eremophilane type — eremophilene lactam (*I*). From the mother liquors a not yet closely studies mixture was isolated, containing substances of the same type, of the composition $C_{15}H_{23}NO_2$ (*III*) and $C_{15}H_{23}NO_3$ (*IV*).

Although it has been known for a long time that the plants of the *Senecioneae* tribe contain alkaloids, nitrogen containing compounds were isolated from the Petasites genus only recently. Japanese authors[1] isolated from *P. japonicus* (SIEB. *et* ZUCC.) MAXIM. two alkaloids of pyrrolizidine type, *i.e.* petasitenine and its acetyl derivative neopetasitenine.

On repeated isolation[2] of some substances of eremophilane type from *P. hybridus* a nitrogen containing analogue of eremophilenolide was isolated and its structure determined. On chromatography of a light petroleum extract of the mentioned plant on silica gel substance *I* was isolated from the polar fractions. Its composition, $C_{15}H_{23}NO$, was also confirmed by mass spectrometry. Its UV spectrum, displaying $\lambda_{max}$ at 221, indicates the presence of a conjugated carbonyl group. From its IR spectrum (frequencies at 3464 $cm^{-1}$ for an —NH-group and 3220 $cm^{-1}$ for the associated form, and bands at 1703·2 $cm^{-1}$ and 1688·4 $cm^{-1}$) it follows that it is a lactam group. The $^1H$-NMR spectrum (100 MHz) showed characteristic signals, typical of substances of eremophilenolide type, and hence it could be assumed that compound *I* also probably had a structure of this type, *i.e.* that it is eremophilene lactam. This assumption was also confirmed by comparison of the characteristic signals in the $^1H$-NMR spectra of eremophilene lactam *I* and eremophilenolide *II* (Table I). The sole important difference was in the chemical shift of the signal $H_{(8)}$ which is, of course, caused by the primary different electronegativity of the lactam and lactone groups.

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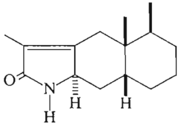
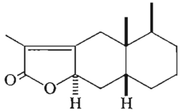
[*] Part CCXLVII in the series On Terpenes; Part CCXLVI: This Journal *42*, 2217 (1977).



*I*



*II*

Hydrogen at $C_8$ in formulas *I* and *II* is incorrectly indicated as α. The correct configuration is β.

Further crystalline fractions were obtained from the mother liquors after crystallization of eremophilene lactam. Mass spectral measurements indicated that they were mixtures of substances $C_{15}H_{23}NO_2$ (*III*) and $C_{15}H_{23}NO_3$ (*IV*). Compound *IV* prevailed in the mixture. The IR spectrum had an absorption maximum at carbonyl group frequency (1 707 $cm^{-1}$), but no band for the hydroxyl group.

## EXPERIMENTAL

The melting points were measured on a Kofler block. The infrared spectra were measured on a Unicam SP-200 spectrometer and a Perkin-Elmer 621 instrument. The UV spectrum was measured with an Optica, Milano, spectrophotometer. The mass spectrum was measured using an AEI-MS 902 spectrometer. For thin-layer chromatography silica gel G according to Stahl (Merck) was employed. Detection was carried out by spraying the plates with conc. sulfuric acid and heating with direct flame. Silica gel of Hermann (Köln, GFR), deactivated with 13% of water, was used for column chromatography.

TABLE I

Comparison of Characteristic Signals of the $^1$H-NMR Spectra of Eremophilene Lactam *I* and Eremophilenolide *II*

| Proton | $I^{c,d}$ | $II^{a,b}$ |
|---|---|---|
| $H_{(6)}$ | 2·85 d ($J_{6,6'} = 14·4$) | 2·88 d ($J_{6,6'} = 14·5$) |
| $H_{(6')}$ | 1·80 dq$^c$ | 1·82$^c$dq |
| $H_{(8)}$ | 3·88 m | 4·61 m |
| $H_{(13)}$ | 1·78 t ($J_{13,8} = J_{13,6} = 1·45$) | 1·78 t ($J_{13,8} = J_{13,6} = 1·45$) |
| $H_{(14)}$ | 0·78 d ($J_{4,14} = 5·8$) | 0·79 d ($J_{4,14} \sim 6$) |
| $H_{(15)}$ | 1·01 s | 1·02 s |

[a] Measured on a Varian HA-100 spectrometer, in deuteriochloroform, data of the first order analysis, chemical shifts in δ-scale, tetramethylsilane as internal reference, splittings in Hz; [d] NH 7·18; [b] data from a 100 MHz instrument; in ref.[3] the data are from a 40 MHz instrument; [c] found by decoupling experiments.

## Isolation of the Substance

The rhizomes of *P. hybridus*, dried at room temperature, were extracted with light petroleum. The crude extract (96·3 g) was separated on silica gel put into a cylindrical kettle, by percolation. First 20 l of benzene were used, followed by 8 l of a benzene–ether 1 : 1 mixture, and then ether alone (20 l). In the last ethereal fractions the first parts of the required substance were eluted, which were then eluted from the column with an ether–methanol 9 : 1 mixture (12 l). The fractions were analysed on thin layers, using chloroform for elution. The total amount of the crude fraction was 8·5 g. This material was rechromatographed on 500 g of silica gel. The column was first eluted with 3 l of a mixture of benzene and ether (1 : 1), then with 2 l of a 4 : 6 mixture of the same solvents, then with 3 l of a 2 : 8 mixture of these solvents, and eventually with 2 l of pure ether. From the last ethereal fractions a substance crystallized out, which after crystallization from benzene or benzene–acetone had m.p. 215—218°C. IR spectrum: 3464, 3220, 1703·2 1688 $cm^{-1}$. UV spectrum: $\lambda_{max}$ 221 nm (log $\varepsilon$ 4·04, methanol). CD spectrum (methanol): $\Delta\varepsilon_{222}$ +11·5. Mass spectrum: $C_{15}H_{23}NO$ 233, 1780; $M^+$ 233, 1790. The peak at mass 124 (base peak) corresponds to the composition $C_6H_{10}NO$, further peaks appear at masses 123, 122, 111, 110, 109 (doublet 5 : 1, $C_6H_7NO$:$C_8H_{18}$), 81 (doublet 1 : 1, $C_5H_7N$:$C_6H_9$). For $C_{15}H_{23}NO$ (233·3) calculated: 77·20% C, 9·94% H, 6·00% N; found: 77·27% C, 9·89% H, 6·08% N. $[\alpha]_D^{22}$ +199·5° (0·33, methanol).

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